```
=> d his

     (FILE 'HOME' ENTERED AT 13:28:25 ON 03 JUN 2002)
               SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 13:28:47 ON 03 JUN 2002
L1             72 S GDF8 OR (GDF OR GROWTH DIFFERENTIAT? FACTOR)()8

     FILE 'REGISTRY' ENTERED AT 13:29:14 ON 03 JUN 2002
L2              1 S 271597-12-7

     FILE 'HCAPLUS' ENTERED AT 13:29:26 ON 03 JUN 2002
L3             24 S L2
L4             72 S L1,L3
                  E KLYSNER S/AU
L5              8 S E3,E4
                  E MOURITSEN S/AU
L6             44 S E3-E5
                  E HALKIER T/AU
L7             69 S E3,E4
                  E PHARMEXA/PA,CS
L8              4 S E3-E8
                  E "M AND B"/PA,CS
                  E "M AND E"/PA,CS
L9              5 S E5-E9
L10            26 S (M(L)"E"(L)BIOTECH?)/PA,CS
L11            14 S (M(1W)"E"(L)BIOTECH?)/PA,CS
L12            14 S L9,L10 AND L11
L13            15 S L9,L11,L12
L14            12 S L10 NOT L13
L15             2 S L4 AND L5-L7
L16             0 S L4 AND L8
L17             1 S L4 AND L13
L18             2 S L15,L17
                  E DK99-1014/AP,PRN
L19             1 S E4
                  E US99-145275/AP,PRN
L20             1 S E5
L21             2 S L18-L20

     FILE 'REGISTRY' ENTERED AT 13:37:37 ON 03 JUN 2002
                  E GROWTH/DIFFERENTIATION FACTOR/CN
L22            50 S E55-E104
L23           132 S GROWTH DIFFERENTIATION FACTOR 8
L24            82 S L23 NOT L2,L22
L25            27 S L24 AND PROTEIN/FS
L26            76 S L22,L23 AND PROTEIN/FS
L27            55 S L22-L25 NOT L2,L26

     FILE 'HCAPLUS' ENTERED AT 13:40:18 ON 03 JUN 2002
L28            21 S L26
L29            15 S L27
L30             1 S L28,L29 AND L5-L7,L13
L31             2 S L21,L30
L32            76 S L4,L28,L29
L33            46 S L32 AND (PD<=19990726 OR PRD<=19990726 OR AD<=19990726)
L34             4 S L33 AND CARRIER
                  E DRUG DELIVERY/CT
                  E E5+ALL
L35             8 S E3,E2+NT AND L33
L36             0 S E342+NT AND L33
L37             1 S E340+NT AND L33
                  E E340+ALL
```

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
jan.delaval@uspto.gov

```
                E E12+ALL
L38          0 S E8+NT AND L33
L39          1 S L33 AND DOWN(L)REGULAT?
                E VACCINE/CT
                E E4+ALL
L40          3 S E4 AND L33
L41          5 S E8+NT AND L33
L42          0 S E10+NT AND L33
L43          0 S E11+NT AND L33
L44         13 S L31,L34,L35,L37,L39-L41
                E MUTATION/CT
                E E3+ALL
L45          8 S L33 AND E1+NT
L46         19 S L44,L45
                E TOXOID/CT
                E E4+ALL
L47          1 S L33 AND E4+NT
L48          3 S L33 AND E3+NT
L49          3 S L33 AND (E8+NT OR E9+NT)
L50         19 S L46-L49
L51         10 S L50 AND GROWTH DIFFERENTIAT? FACTOR
L52         15 S L50 AND GDF?
L53         17 S L51,L52
L54          2 S L50 NOT L53
L55         44 S MYOSTATIN? AND L32
L56         20 S L55 AND L33
L57          1 S L56 AND L31
L58         43 S MYOSTATIN? AND (PD<=19990726 OR AD<=19990726 OR PRD<=19990726

    FILE 'REGISTRY' ENTERED AT 13:53:26 ON 03 JUN 2002
L59        161 S MYOSTATIN?
L60        126 S L59 NOT L2,L22-L27

    FILE 'HCAPLUS' ENTERED AT 13:53:53 ON 03 JUN 2002
L61         14 S L60
L62         27 S L59
L63         27 S L61,L62
L64         18 S L63 AND (PD<=19990726 OR AD<=19990726 OR PRD<=19990726)
L65          5 S L64 AND L50
L66         32 S L50-L54,L56,L57,L65
L67         38 S L33,L58,L64 NOT L66
L68          8 S (L2 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27  OR L59)(L)THU/
L69          7 S L68 AND L66
L70          1 S L68 AND L67
L71          9 S 15/SC,SX AND L33,L58,L64
L72         34 S L69,L71,L66
L73         36 S L67 NOT L72
L74        116 S GROWTH(S)DIFFERENTIATION(S)FACTOR(S)8
L75         76 S L74 AND (PD<=19990726 OR PRD<=19990726 OR AD<=19990726)
L76         47 S L75 NOT L33,L58,L64
L77         19 S L74 AND L72
L78         34 S L72,L77
L79         21 S L78 AND GROWTH(L)DIFFERENTIATION(L)FACTOR
L80         13 S L78 NOT L79
                SEL DN 4 7 9
L81          3 S E1-E3 AND L80
                SEL DN 1 7 9 11 15 16 21 L79
L82         14 S L79 NOT E4-E10
L83         16 S L81,L82 AND GROWTH(L)DIFFERENT?(L)FACTOR
L84         17 S L81,L82 AND L1,L2-L21,L28-L58,L61-L83
                SEL HIT RN

    FILE 'REGISTRY' ENTERED AT 15:00:02 ON 03 JUN 2002
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L85          145 S E11-E155
L86            1 S L85 AND L2
L87           42 S L85 AND L22-L27
L88          109 S L85 AND L59,L60
L89          113 S L87,L88 AND PROTEIN/FS
L90           21 S L89 AND GROWTH(L)DIFFERENTIATION(L)FACTOR(L)8/CNS
L91           92 S L89 NOT L90
L92           31 S L85 NOT L86,L89-L91
L93           20 S L92 AND GROWTH(L)DIFFERENTIATION(L)FACTOR(L)8/CNS
L94           11 S L92 NOT L93
L95           18 S L93 NOT MYOSTATIN/INS.HP
L96           40 S L90,L95,L86
L97           38 S L96 NOT MYOSTATIN/INS.HP
L98           37 S L97 NOT L86

=> fil reg
FILE 'REGISTRY' ENTERED AT 15:06:26 ON 03 JUN 2002
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STRUCTURE FILE UPDATES:    2 JUN 2002  HIGHEST RN 424787-52-0
DICTIONARY FILE UPDATES:   2 JUN 2002  HIGHEST RN 424787-52-0

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide can l2

L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   271597-12-7  REGISTRY
CN   Growth/differentiation factor 8 (9CI)  (CA INDEX NAME)
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
              23 REFERENCES IN FILE CA (1967 TO DATE)
              24 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  136:322627

REFERENCE   2:  136:260726

REFERENCE   3:  136:172724

REFERENCE   4:  136:116753

REFERENCE   5:  136:35184

REFERENCE   6:  135:327574

REFERENCE   7:  135:105367
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REFERENCE 8: 135:90448

REFERENCE 9: 135:14644

REFERENCE 10: 134:290751

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 15:06:38 ON 03 JUN 2002

FILE COVERS 1907 - 3 Jun 2002 VOL 136 ISS 23
FILE LAST UPDATED: 31 May 2002 (20020531/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d all tot l84

L84 ANSWER 1 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:64021 HCAPLUS
DN 134:130255
TI Method for **down-regulating GDF-8** activity
IN **Halkier, Torben; Mouritsen, Soren; Klysner, Steen**
PA **M and E Biotech A/S, Den.**
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-00
CC **15-2** (Immunochemistry)
Section cross-reference(s): 2, 3, 5, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001005820	A2	20010125	WO 2000-DK413	20000720 <--
	WO 2001005820	A3	20010719		

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR,

TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1200119 A2 20020502 EP 2000-945671 20000720 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL
PRAI DK 1999-1014 A 19990720 <--
US 1999-145275P P 19990726 <--
WO 2000-DK413 W 20000720

AB Disclosed are novel methods for increasing muscle mass by means of immunization against **growth differentiation factor 8** (**GDF-8**, **myostatin**). Immunization is preferably effected by administration of analogs of **GDF-8** which are capable of inducing antibody prodn. against homologous **GDF-8**. Esp. preferred as an immunogen is homologous **GDF-8** which has been modified by introduction of one single or a few foreign, immunodominant and promiscuous T-cell epitopes while substantially preserving the tertiary structure of the homologous **GDF-8**. Also disclosed are nucleic acid vaccination against **GDF-8** and vaccination using live vaccines as well as methods and means useful for the vaccination. Such methods and means include methods for identification of useful immunogenic **GDF-8** analogs, methods for the prepn. of analogs and pharmaceutical formulations, as well as nucleic acid fragments, vectors, transformed cells, polypeptides and pharmaceutical formulations.

ST **growth differentiation factor 8**
muscle mass; vaccine **GDF8** farm animal muscle mass

IT **Antigens**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**CS** (circumsporozoite); chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Hematopoietin receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FLT3 receptors; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Heat-shock proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HSP 70; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Heat-shock proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HSP 90; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Histocompatibility antigens**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MHC (major histocompatibility complex), class II; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Diglycerides
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(N-acyl; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(P2; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(P30; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Animal cell line
(S2; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Animal cell line
(SF; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Encapsulants
(adjuvant; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT DNA
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjuvant; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Immunostimulants**
(adjuvants, ISCOMs; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Immunostimulants**
(adjuvants; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(anal; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Immune tolerance
(auto-; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Antigens**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(autoantigens; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(buccal; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Reagents
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(calcium-pptg.; chimeric vaccines for **down-regulation**

of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(**carriers**; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Animal
Animal cell line
Antigen-presenting cell
B cell (lymphocyte)
Bacillus (bacterium genus)
Bacteriophage
Bacterium (genus)
Cattle
Chicken (Gallus domesticus)
Cosmids
Epitopes
Escherichia
Escherichia coli
Eukaryote (Eukaryotae)
Fungi
Genetic vectors
Genome
Immunostimulants
Influenza virus
Insect (Insecta)
Livestock
Micelles
Microorganism
Mycobacterium
Mycobacterium bovis
Particles
Plant cell
Plasmids
Plasmodium falciparum
Poultry
Poxviridae
Prokaryote
Protein sequences
Protozoa
Salmonella
Sheep
Swine
Turkey
Vaccines
Vaccinia virus
Virus vectors
Yeast
(chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Antibodies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Fusion proteins (chimeric proteins)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in

farm animals)
IT Calreticulin
Carbohydrates, biological studies
Cytokines
Haptens
Heat-shock proteins
Hemagglutinins
Hormones, animal, biological studies
Interleukin 1
Interleukin 12
Interleukin 13
Interleukin 15
Interleukin 2
Interleukin 4
Interleukin 6
Leader peptides
Lipids, biological studies
Nucleic acids
Polymers, biological studies
Promoter (genetic element)
Receptors
Saponins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)
IT **Mutation**
(deletion; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)
IT **Toxoids**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diphtheria; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)
IT Glycophosphoproteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(endoplasmins; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)
IT **Drug delivery systems**
(epidural; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)
IT T cell (lymphocyte)
(epitope; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)
IT T cell (lymphocyte)
(helper cell, epitope; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)
IT Phosphoproteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hsc 70 (heat-shock cognate, 70,000-mol.-wt.); chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)
IT **Carriers**
Molecules

(inert; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(injections, i.m.; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(injections, i.v.; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(injections, s.c.; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Mutation**
(insertion; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(intraarterial; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(intracranial; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(intracutaneous; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(intradermal; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(liposomes; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Animal cell
(mammalian; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Muscle
(mass; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Chromosome
(minichromosomes; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(oil formulation; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(oral; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(parenterals; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(peritoneal; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Glycolipoproteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphatidylinositol-contg.; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(spinal; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(subdermal; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Drug delivery systems**
(sublingual; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Mutation**
(substitution; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Antigens**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surface; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Genetic element
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(terminator; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **Toxoids**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tetanus; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transfection-facilitating; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Lymph node
(virtual lymph node device; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT Interferons
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma.; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT 7429-90-5D, Aluminum, derivs., biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(adjuvant; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **161135-86-0, Growth/differentiation factor 8** (human) **211433-36-2, Growth /differentiation factor 8** (cattle) **321893-41-8 321893-42-9 321893-43-0 321893-44-1 321893-45-2 321893-46-3 321893-47-4 321893-48-5 321893-49-6 321893-50-9 321893-51-0**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **271597-12-7, Growth differentiation factor 8** 321856-81-9 321856-82-0 321856-83-1 321856-84-2 321856-85-3 321856-86-4 321856-87-5 321856-88-6 321856-89-7 321856-90-0 321856-91-1
RL: BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT 112-18-5, DDA 1398-61-4, Chitin 3458-28-4, Mannose 9012-76-4, Chitosan 9036-88-8, Mannan 83869-56-1, GM-CSF
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pptg. agent; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

IT **161135-84-8 199810-42-9, Myostatin** (cattle muscle gene MSTN) **199810-43-0, Myostatin** (chicken muscle gene MSTN) **199810-44-1, Myostatin** (sheep muscle gene MSTN) **199810-45-2, Myostatin** (swine muscle gene MSTN) **199810-46-3 199810-47-4, Myostatin** (turkey muscle gene MSTN) **199810-48-5, Myostatin** (Danio rerio muscle gene MSTN)
RL: PRP (Properties)
(unclaimed protein sequence; method for **down-regulating GDF-8** activity)

IT 126779-13-3 126779-14-4
RL: PRP (Properties)
(unclaimed sequence; method for **down-regulating GDF-8** activity)

IT 9005-80-5, Inulin
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma.-; chimeric vaccines for **down-regulation** of **GDF-8** activity and for increase of muscle mass in farm animals)

L84 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:900806 HCAPLUS
DN 134:67212
TI Sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression

IN Wu-Wong, Jinshyun R.; Wang, Jiahong
PA Abbott Laboratories, USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-12
ICS C12N005-10; C07K014-475; C07K016-18; G01N033-50; G01N033-566; C12Q001-68
CC 3-4 (Biochemical Genetics)
Section cross-reference(s): 1, 13
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000077206	A2	20001221	WO 2000-US15868	20000609 <--
	WO 2000077206	A3	20011206		
	W: CA, JP, MX				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6284882	B1	20010904	US 1999-329685	19990610 <--
	EP 1185649	A2	20020313	EP 2000-941296	20000609 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 2001049435	A1	20011206	US 2001-901511	20010709 <--
PRAI	US 1999-329685	A	19990610 <--		
	WO 2000-US15868	W	20000609		

AB The present invention provides DNA sequence of a human promoter which induces expression of the **myostatin** gene, and methods for identifying compns. useful for the inhibition of the promoter, and also methods and compns. useful for preventing the synthesis, secretion and function of **myostatin**. In particular, inhibitors that prevent the synthesis, secretion and function of **myostatin** may be used to prevent the loss of muscle mass in humans and animals.
ST human **myostatin** gene promoter sequence
IT Genetic vectors
(comprising **myostatin** gene promoter operably linked to reporter gene; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)
IT Bioassay
(for identifying a compn. which prevents **myostatin** from binding to a **myostatin** receptor; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)
IT Genetic methods
(for identifying compns. which inhibits activation of **myostatin** gene promoter; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)
IT Reporter gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for **myostatin** gene promoter activation; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)
IT Promoter (genetic element)
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(for **myostatin** gene; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)
IT Muscle
(**myostatin** mRNA in; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**myostatin**, regulation the expression of; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)
IT mRNA
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(of **myostatin** gene, tissue distribution; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)
IT Myoma
(rhabdomyosarcoma, **myostatin** mRNA in; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)
IT DNA sequences
(sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)
IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(to **myostatin**; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)
IT Muscle, disease
(wasting, preventing; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)
IT 9014-00-0, Luciferase 9031-11-2, .beta.-Galactosidase 9040-07-7, Chloramphenicol acetyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene for, as reporter gene; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)
IT **271597-12-7, Growth/differentiation factor 8**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**myostatin**; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)
IT **314085-29-5**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(nucleotide sequence; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)
IT 314099-90-6 314329-00-5
RL: PRP (Properties)
(unclaimed sequence; sequence of human **myostatin** gene promoter and uses in inhibition **myostatin** gene expression)

L84 ANSWER 3 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:531604 HCAPLUS
DN 133:149138
TI Antibodies specific for **growth differentiation factor-8** and methods of using same
IN Lee, Se-Jin; McPherron, Alexandra C.
PA The Johns Hopkins University School of Medicine, USA
SO U.S., 45 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07K016-22
ICS G01N033-53
NCL 435007100
CC **15-3** (Immunochemistry)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6096506	A	20000801	US 1998-177860	19981023 <--

AB **Growth differentiation factor-8** (**GDF-8**) is disclosed along with its polynucleotide sequence and amino acid sequence. Also disclosed are diagnostic and therapeutic methods of using the **GDF-8** polypeptide and polynucleotide sequences. The antibodies may be polyclonal or monoclonal antibodies and are useful for treating cell proliferative disorders of muscle, nerve and adipose tissue.

ST **GDF8** monoclonal antibody cell proliferative disorder; **growth differentiation factor 8** polyclonal antibody; muscle nerve adipose proliferative disease **GDF8**

IT Chemiluminescent substances
DNA sequences
Epitopes
Fluorescent substances
Labels
Protein sequences
(antibodies specific for **growth differentiation factor-8** for treating cell proliferative disease of muscle, nerve or adipose tissue)

IT Radionuclides, biological studies
RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(antibodies specific for **growth differentiation factor-8** for treating cell proliferative disease of muscle, nerve or adipose tissue)

IT Antibodies
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antibodies specific for **growth differentiation factor-8** for treating cell proliferative disease of muscle, nerve or adipose tissue)

IT Luminescent substances
(bioluminescent; antibodies specific for **growth differentiation factor-8** for treating cell proliferative disease of muscle, nerve or adipose tissue)

IT Muscle, disease
Nerve, disease
(cell proliferative disorder; antibodies specific for **growth differentiation factor-8** for treating cell proliferative disease of muscle, nerve or adipose tissue)

IT Muscle
(cell sample; antibodies specific for **growth differentiation factor-8** for treating cell proliferative disease of muscle, nerve or adipose tissue)

IT Adipose tissue
(disease, cell proliferative disorder; antibodies specific for **growth differentiation factor-8** for treating cell proliferative disease of muscle, nerve or adipose tissue)

IT **Growth factors**, animal
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**growth differentiation factor 8** or **GDF-8**; antibodies specific for **growth differentiation factor-8** for treating cell proliferative disease of muscle, nerve or adipose tissue)

IT Antibodies

RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal; antibodies specific for **growth differentiation factor-8** for treating cell proliferative disease of muscle, nerve or adipose tissue)

IT Disease, animal
(proliferative, cell; antibodies specific for **growth differentiation factor-8** for treating cell proliferative disease of muscle, nerve or adipose tissue)

IT Animal tissue
Body fluid
(sample; antibodies specific for **growth differentiation factor-8** for treating cell proliferative disease of muscle, nerve or adipose tissue)

IT **161135-84-8P 161135-86-0P**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; antibodies specific for **growth differentiation factor-8** for treating cell proliferative disease of muscle, nerve or adipose tissue)

IT **271597-12-7P, Growth/differentiation factor 8**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(antibodies specific for **growth differentiation factor-8** for treating cell proliferative disease of muscle, nerve or adipose tissue)

IT **161135-83-7 161135-85-9**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(nucleotide sequence; antibodies specific for **growth differentiation factor-8** for treating cell proliferative disease of muscle, nerve or adipose tissue)

IT **243706-30-1**, 5: PN: US6096506 SEQID: 5 unclaimed DNA
243706-31-2, **8**: PN: US6096506 SEQID: 7 unclaimed DNA
285573-29-7, 1: PN: US6090563 SEQID: 1 unclaimed DNA 286481-43-4, 2: PN: US6096506 SEQID: 2 unclaimed DNA 286481-44-5, 3: PN: US6096506 SEQID: 3 unclaimed DNA 286481-45-6, 4: PN: US6096506 SEQID: 4 unclaimed DNA
286481-48-9 286481-49-0 286481-50-3
RL: PRP (Properties)
(unclaimed nucleotide sequence; antibodies specific for **growth differentiation factor-8** and methods of using same)

IT 138675-14-6, **8**-126-Glycoprotein OP 1 (human clone HH(dT+R)-1 osteogenic short isoform protein moiety reduced) 285573-32-2
285573-33-3 285573-34-4 285573-35-5 285573-36-6 285573-37-7
285573-38-8 285573-39-9 285577-96-0 285577-97-1 285577-98-2
285577-99-3 285988-67-2 **286481-46-7 286481-47-8**
286481-51-4 286849-74-9 286849-79-4
RL: PRP (Properties)
(unclaimed protein sequence; antibodies specific for **growth differentiation factor-8** and methods of using same)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Alexandra, C; The Journal of Biological Chemistry 1993, V268(5), P3444
(2) Bowie; Science 1990, V247, P1307
(3) Callard; The Cytokine FactsBook 1994, P31
(4) Jones; Molecular Endocrinology 1992, V6(11), P1961 HCAPLUS
(5) Lee; US 5827733 1998 HCAPLUS

(6) Ngo; The Protein Folding Problem and Tertiary Structure Prediction 1990, P491
(7) Rudinger; Peptide Hormones 1976, P1
(8) Se-Jin, L; Molecular Endocrinology 1990, V4, P1034
(9) Se-Jin, L; Proc Natl Acad Sci USA 1991, V88, P4250
(10) Wells; Biochemistry 1990, V29, P8507

L84 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:513895 HCAPLUS
DN 133:129841
TI **Growth** and **differentiation factor** inhibitors and uses therefor
IN Topouzis, Stavros; Wright, Jill F.; Ratovitski, Tamara; Liang, Li-Fang; Brady, James L., Jr.; Sinha, Debasish; Yaswen-Corkery, Linda
PA Metamorphix, Inc., USA
SO PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N033-50
ICS G01N033-68; C07K014-51; C07K014-475; C07K007-08; C07K007-06; A01K067-027; C12N009-00; C12N015-11
CC 1-1 (Pharmacology)
Section cross-reference(s): **15**

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000043781	A2	20000727	WO 2000-US1552	20000121 <--
WO 2000043781	A3	20010201		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1147413	A2	20011024	EP 2000-903387	20000121 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008188	A	20020213	BR 2000-8188	20000121 <--
PRAI US 1999-116639P	A2	19990121 <--		
US 1999-138363P	A2	19990610 <--		
WO 2000-US1552	W	20000121		

AB Inhibitors of GDF proteins, such as **GDF-8** or GDF-11, are disclosed. Also disclosed are methods for identifying and using the inhibitors, for example, to generate transgenic animals and to treat a variety of diseases.

ST **growth differentiation factor** inhibitor drug screening
IT Muscle
(-specific enzymes; **growth** and **differentiation factor** inhibitors for therapeutic use)
IT Animal cell line
(CHO, mol. cloning in; **growth** and **differentiation factor** inhibitors for therapeutic use)
IT Baboon
Cattle
Chicken (Gallus domesticus)
Mouse
Rat
Sheep

Swine
Turkey
(GDF of; **growth** and **differentiation factor** inhibitors for therapeutic use)

IT Transforming **growth factors**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(GDF-11 (**growth** and **differentiation factor** -11), inhibitors; **growth** and **differentiation factor** inhibitors for therapeutic use)

IT Transforming **growth factors**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(**GDF-8** (**growth** and **differentiation factor-8**), inhibitors; **growth** and **differentiation factor** inhibitors for therapeutic use)

IT Antibodies
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); USES (Uses)
(GDF-inhibitory; **growth** and **differentiation factor** inhibitors for therapeutic use)

IT Polyacrylamide gel electrophoresis
(SDS-; **growth** and **differentiation factor** inhibitors for therapeutic use)

IT Adipose tissue
(adipocyte, **differentiation**; **growth** and **differentiation factor** inhibitors for therapeutic use)

IT Cell **differentiation**
(adipocyte; **growth** and **differentiation factor** inhibitors for therapeutic use)

IT Transcription, genetic
(assays; **growth** and **differentiation factor** inhibitors for therapeutic use)

IT Animal tissue culture
Culture media
Drug screening
Glycosylation
Ion exchange chromatography
Molecular weight distribution
Myoblast
Plasmid vectors
Protein sequences
Reversed phase chromatography
Transformation, genetic
cDNA sequences
(**growth** and **differentiation factor** inhibitors for therapeutic use)

IT T cell (lymphocyte)
(immune response; **growth** and **differentiation factor** inhibitors for therapeutic use)

IT Enzymes, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(muscle-specific; **growth** and **differentiation factor** inhibitors for therapeutic use)

IT Cell **differentiation**
(of adipocytes; **growth** and **differentiation factor** inhibitors for therapeutic use)

IT Adipose tissue
(preadipocyte, 3T3-L1; **growth** and **differentiation factor** inhibitors for therapeutic use)
IT 151-21-3, Sds, uses
RL: NUU (Other use, unclassified); USES (Uses)
(-PAGE; **growth** and **differentiation factor** inhibitors for therapeutic use)
IT 9001-75-6, Pepsin 9001-92-7, Proteinase 9002-07-7, Trypsin 9004-07-3, Chymotrypsin 9073-78-3, Thermolysin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**growth** and **differentiation factor** inhibitors for therapeutic use)
IT 286435-12-9 286435-13-0 286435-14-1 286435-15-2 286435-16-3 286435-17-4 286451-10-3 286451-11-4 286451-12-5 286451-13-6 286451-14-7 286451-15-8 286451-16-9 286451-17-0 286451-18-1 286451-19-2 286451-20-5 286451-21-6 286451-22-7 286451-23-8 286451-24-9 286451-25-0 286451-26-1 286451-27-2 286451-28-3 286451-29-4 286451-30-7 286451-31-8 286451-32-9 286451-33-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**growth** and **differentiation factor** inhibitors for therapeutic use)
IT 9001-15-4, Creatine kinase
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**growth** and **differentiation factor** inhibitors for therapeutic use)
IT 286452-56-0, 46: PN: WO0043781 FIG: 13 unclaimed DNA 286452-58-2, 50: PN: WO0043781 FIG: 18 unclaimed DNA 286452-59-3, 51: PN: WO0043781 FIG: 19 unclaimed DNA 286452-60-6, 52: PN: WO0043781 FIG: 19 unclaimed DNA 286452-61-7, 53: PN: WO0043781 FIG: 19 unclaimed DNA 286452-62-8, 54: PN: WO0043781 FIG: 19 unclaimed DNA 286452-63-9, 55: PN: WO0043781 FIG: 19 unclaimed DNA 286452-64-0, 56: PN: WO0043781 FIG: 19 unclaimed DNA 286452-65-1, 57: PN: WO0043781 FIG: 19 unclaimed DNA 286452-66-2, 58: PN: WO0043781 FIG: 19 unclaimed DNA 286452-67-3, 59: PN: WO0043781 FIG: 20 unclaimed DNA 286452-69-5, 61: PN: WO0043781 FIG: 22 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; **growth** and **differentiation factor** inhibitors and uses therefor)
IT **161135-86-0** 286452-57-1 286452-68-4
RL: PRP (Properties)
(unclaimed protein sequence; **growth** and **differentiation factor** inhibitors and uses therefor)
IT **161135-84-8 199810-43-0, Myostatin** (chicken muscle gene MSTN) 286452-48-0 286452-49-1 286452-50-4 286452-51-5 286452-52-6 286452-53-7 286452-54-8 286452-55-9
RL: PRP (Properties)
(unclaimed sequence; **growth** and **differentiation factor** inhibitors and uses therefor)

L84 ANSWER 5 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:351383 HCAPLUS
DN 133:13162
TI Methods of alleviating cancer symptoms using a morphogen
IN Sampath, Kuber T.; Cohen, Charles M.; Rueger, David C.
PA Creative Biomolecules, Inc., USA
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-18

ICS A61P035-00
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000029012	A2	20000525	WO 1999-US26636	19991112 <--
	WO 2000029012	A3	20001116		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	EP 1131087	A2	20010912	EP 1999-958892	19991112 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRAI	US 1998-191239	A2	19981113	<--
	WO 1999-US26636	W	19991112	

AB The invention provides methods for alleviating the symptoms of cancer by administering a morphogen. The present invention also provides compns. and methods for the inhibition or prevention of unchecked growth of cancer cells or for the stimulation of differentiation of cancer cells away from their particular cancer phenotype. The morphogen comprises a dimeric protein having an amino acid sequence selected from the group consisting of a sequence: (a) having at least 70% amino acid homol. with the C-terminal seven-cysteine skeleton of human OP-1, residues 330-431, and (b) having at least 60% amino acid sequence identity with the C-terminal seven cysteine skeleton of human OP-1. The morphogen is selected from the group consisting of OP-1, OP-2, OP-3, BMP-2, BMP-3, BMP-3b, BMP-4, BMP-5, BMP-6, BMP-9, BMP-10, BMP-11, BMP-12, BMP-13, BMP-14, BMP-15, DPP, Vg1, Vgr-1, 60A protein, CDMP-1,CDMP-2, CDMP-3, **GDF**-1, **GDF**-3, **GDF**-5, **GDF**-6, **GDF**-7, **GDF**-8, **GDF**-9, **GDF**-10, **GDF11**, **GDF**-12, NODAL, UNIVIN, SCREW, ADMP, NEURAL, and morphogenically active amino acid sequence variants thereof. The morphogen may be non-covalently assocd. with at least one pro-domain polypeptide selected from the group consisting of the pro-domains of OP-1, OP-2, 60A, **GDF**-1, BMP-2A, BMP-2B, DPP, Vg1, Vgr-1, BMP-3, BMP-5, and BMP-6. Noninfectious, non-integrating DNA encoding the desired morphogen can also be administered. The cancer to be treated is selected from the group consisting of adrenal cancer, anus cancer, bladder cancer, bone cancer, brain cancer, breast cancer, cervix cancer, colon cancer, corpus cancer, endocrine cancer, esophageal cancer, fallopian tube cancer, fat cell cancer, gall bladder cancer, germ cell tumors, gastrointestinal tract cancer, kidney cancer, leukemia, liver cancer, lymphoma, lung cancer, muscle cancer, nervous system cancer, ocular tissue cancer, oral cancer, ovarian cancer, pancreatic cancer, prostate cancer, rectal cancer, skin cancer, small intestine cancer, soft tissue cancer, stomach cancer, teratocarcinoma, testicular cancer, thyroid cancer, ureteral cancer, urinary cancer, uterine cancer, and metastatic cancer of unknown primary site. The morphogens can be administered in combination with another therapeutic agent, e.g., another antitumor agent.

ST cancer treatment morphogen; drug formulation cancer treatment morphogen
IT Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(10; methods of alleviating cancer symptoms using a morphogen)
IT Bone morphogenetic proteins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(11; methods of alleviating cancer symptoms using a morphogen)

IT Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(12; methods of alleviating cancer symptoms using a morphogen)

IT Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(13; methods of alleviating cancer symptoms using a morphogen)

IT Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(14; methods of alleviating cancer symptoms using a morphogen)

IT Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(15; methods of alleviating cancer symptoms using a morphogen)

IT Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2; methods of alleviating cancer symptoms using a morphogen)

IT Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2A; methods of alleviating cancer symptoms using a morphogen)

IT Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3, 3b; methods of alleviating cancer symptoms using a morphogen)

IT Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3; methods of alleviating cancer symptoms using a morphogen)

IT Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(4; methods of alleviating cancer symptoms using a morphogen)

IT Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5; methods of alleviating cancer symptoms using a morphogen)

IT Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(6; methods of alleviating cancer symptoms using a morphogen)

IT Bone morphogenetic proteins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(7; methods of alleviating cancer symptoms using a morphogen)

IT Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(9; methods of alleviating cancer symptoms using a morphogen)
IT Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ADMP; methods of alleviating cancer symptoms using a morphogen)
IT Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NEURAL; methods of alleviating cancer symptoms using a morphogen)
IT Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NODAL; methods of alleviating cancer symptoms using a morphogen)
IT Bone morphogenetic proteins
Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(OP-3; methods of alleviating cancer symptoms using a morphogen)
IT Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SCREW; methods of alleviating cancer symptoms using a morphogen)
IT Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(UNIVIN; methods of alleviating cancer symptoms using a morphogen)
IT Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Vgl; methods of alleviating cancer symptoms using a morphogen)
IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Vgr-1 (Vgl-related); methods of alleviating cancer symptoms using a morphogen)
IT Adipose tissue
(adipocyte, cancer, inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Intestine
(anus, cancer, inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(bladder carcinoma; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
Antitumor agents
(bone; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
Antitumor agents
(brain; methods of alleviating cancer symptoms using a morphogen)
IT Bladder

Bladder
(carcinoma, inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Uterus, neoplasm
Uterus, neoplasm
(cervix, inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(cervix; methods of alleviating cancer symptoms using a morphogen)
IT Intestine, neoplasm
Intestine, neoplasm
(colon, inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(colon; methods of alleviating cancer symptoms using a morphogen)
IT Intestine, neoplasm
(colorectal, inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(digestive tract; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(esophagus; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
Antitumor agents
(eye; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(for corpus cancer; methods of alleviating cancer symptoms using a morphogen)
IT Liver, neoplasm
Liver, neoplasm
(hepatoma, inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(hepatoma; methods of alleviating cancer symptoms using a morphogen)
IT Adrenal gland, neoplasm
Bone, neoplasm
Bone, neoplasm
Brain, neoplasm
Brain, neoplasm
Eye, neoplasm
Eye, neoplasm
Kidney, neoplasm
Kidney, neoplasm
Lung, neoplasm
Lung, neoplasm
Myoma
Myoma
Ovary, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Pancreas, neoplasm
Skin, neoplasm
Skin, neoplasm
Stomach, neoplasm
Stomach, neoplasm
Testis, neoplasm
Testis, neoplasm
Thyroid gland, neoplasm
Thyroid gland, neoplasm
Uterus, neoplasm
Uterus, neoplasm
(inhibitors; methods of alleviating cancer symptoms using a morphogen)

IT Antitumor agents
Antitumor agents
(kidney; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(leukemia; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
Antitumor agents
(lung; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(lymphoma; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(mammary gland; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(metastasis; methods of alleviating cancer symptoms using a morphogen)
IT **Drug delivery systems**
(methods of alleviating cancer symptoms using a formulation contg. a morphogen)
IT Antitumor agents
(methods of alleviating cancer symptoms using a morphogen)
IT **Drug delivery systems**
(microspheres; methods of alleviating cancer symptoms using a formulation contg. a morphogen)
IT Antitumor agents
(mouth; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
Antitumor agents
(myoma inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Gallbladder
(neoplasm, cancer, inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Digestive tract
Digestive tract
Endocrine system
Esophagus
Esophagus
Mammary gland
Mammary gland
Mouth
Mouth
Oviduct
Prostate gland
Prostate gland
Ureter
Ureter
Urinary tract
Urinary tract
(neoplasm, inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
Antitumor agents
(nervous system tumor inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteogenic protein 2; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
Antitumor agents
(ovary; methods of alleviating cancer symptoms using a morphogen)

IT Antitumor agents
Antitumor agents
(pancreas; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(prostate gland; methods of alleviating cancer symptoms using a morphogen)
IT Intestine, neoplasm
(rectum, inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(rectum; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
Antitumor agents
(skin; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(small intestine; methods of alleviating cancer symptoms using a morphogen)
IT Intestine, neoplasm
Intestine, neoplasm
(small, inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Animal tissue
(soft, cancer, inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT **Drug delivery systems**
(solns.; methods of alleviating cancer symptoms using a formulation contg. a morphogen)
IT Antitumor agents
Antitumor agents
(stomach; methods of alleviating cancer symptoms using a morphogen)
IT Carcinoma
(teratocarcinoma, inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
Antitumor agents
(testis; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
Antitumor agents
(thyroid; methods of alleviating cancer symptoms using a morphogen)
IT Nervous system
Nervous system
(tumor inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Gamete and Germ cell
(tumor, inhibitors; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(ureter; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
(urinary tract; methods of alleviating cancer symptoms using a morphogen)
IT Antitumor agents
Antitumor agents
(uterus; methods of alleviating cancer symptoms using a morphogen)
IT Gene therapy
(with a DNA encoding a morphogen; methods of alleviating cancer symptoms using a morphogen)
IT 129805-33-0 193830-08-9, **Growth/differentiation factor** 5 193830-09-0, **Growth/differentiation factor** 6 193830-10-3, **Growth/differentiation factor** 7 208778-50-1, **Growth/differentiation factor** 9 244293-01-4, PN: WO9947156 SEQID: 3 unclaimed protein 244293-02-5, PN: WO9947156 SEQID: 4 unclaimed protein 244293-03-6, PN:

WO9947156 SEQID: 5 unclaimed protein 244293-07-0, PN: WO9947156 SEQID: 6 unclaimed protein 244293-08-1, PN: WO9947156 SEQID: 7 unclaimed protein 252959-51-6, **Growth/differentiation factor** 11 271597-10-5, **Growth/differentiation factor** 1 271597-11-6, **Growth/differentiation factor** 3 **271597-12-7, Growth/differentiation factor 8** 271597-13-8, **Growth/differentiation factor** 10 271597-14-9, **Growth/differentiation factor** 12
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods of alleviating cancer symptoms using a morphogen)

IT 138674-79-0
RL: PRP (Properties)
(unclaimed nucleotide sequence; methods of alleviating cancer symptoms using a morphogen)

IT 244061-42-5
RL: PRP (Properties)
(unclaimed protein sequence; methods of alleviating cancer symptoms using a morphogen)

IT 154768-04-4 154768-05-5 158164-55-7 182894-54-8 209674-93-1, 38-139-Osteogenic protein OP-1 (mouse) 209674-95-3, 38-139-Osteogenic protein OP-2 (mouse) 271754-11-1 271754-12-2 271754-13-3 271754-14-4 271754-15-5 271754-16-6 271754-17-7 271754-18-8 271754-19-9
RL: PRP (Properties)
(unclaimed sequence; methods of alleviating cancer symptoms using a morphogen)

L84 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:68486 HCAPLUS
DN 132:118343
TI **Growth differentiation factor GDF-8** promoter and its uses for tissue-specific gene expression and identification of **GDF** expression regulators
IN Liang, Li-Fang
PA Metamorphix, Inc., USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-00
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 2, 13
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000004051	A2	20000127	WO 1999-US16026	19990715 <--
WO 2000004051	A3	20000525		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9955427	A1	20000207	AU 1999-55427	19990715 <--
EP 1097233	A2	20010509	EP 1999-941954	19990715 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO
PRAI US 1998-92865P P 19980715 <--
US 1999-123270P P 19990308 <--
WO 1999-US16026 W 19990715 <--

AB The complete nucleotide sequences of **GDF** promoters (e.g., **GDF-8** promoters) from human, mouse, chicken, and pig are described. Also described are methods of using the **GDF** promoters to regulate tissue-specific, particularly muscle- specific gene expression, and to identify compds. which regulate **GDF** expression. Expression vector constructs comprising the **GDF-8** gene promoter fused to a gene of interest, possibly a reporter gene are provided.

ST tissue specific gene expression **GDF** regulator; sequence **growth differentiation factor GDF8** promoter human chicken pig

IT Gene
(expression, muscle-specific; **growth differentiation factor GDF-8** promoter and uses for tissue-specific gene expression and identification of **GDF** expression regulators)

IT Chicken (Gallus domesticus)
Mouse (Mus musculus)
Swine
(**growth differentiation factor GDF-8** promoter and uses for tissue-specific gene expression and identification of **GDF** expression regulators)

IT **Growth factors**, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**growth differentiation factor GDF-8** promoter and uses for tissue-specific gene expression and identification of **GDF** expression regulators)

IT Reporter gene
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**growth differentiation factor GDF-8** promoter and uses for tissue-specific gene expression and identification of **GDF** expression regulators)

IT **Drug delivery systems**
(injections, of **GDF** promoter into a muscle cell or transgenic animal; **growth differentiation factor GDF-8** promoter and uses for tissue-specific gene expression and identification of **GDF** expression regulators)

IT Transformation, genetic
(microinjection; **growth differentiation factor GDF-8** promoter and uses for tissue-specific gene expression and identification of **GDF** expression regulators)

IT **Growth factors**, animal
Growth inhibitors, animal
RL: ANT (Analyte); ANST (Analytical study)
(of **GDF** expression; **growth differentiation factor GDF-8** promoter and uses for tissue-specific gene expression and identification of **GDF** expression regulators)

IT Promoter (genetic element)
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process)
(of **growth differentiation factor GDF-8** gene; **growth differentiation factor GDF-8** promoter and uses for tissue-specific gene expression and identification of **GDF**

expression regulators)
IT DNA sequences
(of **growth differentiation factor GDF-8** promoter; **growth differentiation factor GDF-8** promoter and uses for tissue-specific gene expression and identification of **GDF** expression regulators)
IT Genetic vectors
(pGL3-0.65; **growth differentiation factor GDF-8** promoter and uses for tissue-specific gene expression and identification of **GDF** expression regulators)
IT Muscle
(transfection of; **growth differentiation factor GDF-8** promoter and uses for tissue-specific gene expression and identification of **GDF** expression regulators)
IT **256216-14-5P 256216-15-6P 256216-16-7P 256216-17-8P 256216-18-9P 256216-19-0P 256216-20-3P 256216-21-4P**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process)
(nucleotide sequence; **growth differentiation factor GDF-8** promoter and uses for tissue-specific gene expression and identification of **GDF** expression regulators)
IT 256216-88-3, 3: PN: WO0004051 SEQID: 3 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; **growth differentiation factor GDF-8** promoter and its uses for tissue-specific gene expression and identification of **GDF** expression regulators)

L84 ANSWER 7 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:813761 HCAPLUS
DN 132:232567
TI Frequent sequence variation in the human **myostatin** (**GDF8**) gene as a marker for analysis of muscle-related phenotypes
AU Ferrell, Robert E.; Conte, Victor; Lawrence, Elizabeth C.; Roth, Stephen M.; Hagberg, James M.; Hurley, Ben F.
CS Department of Human Genetics, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA, 15261, USA
SO Genomics (**1999**), 62(2), 203-207
CODEN: GNMCEP; ISSN: 0888-7543
PB Academic Press
DT Journal
LA English
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 6, 13
AB **Myostatin** is a recently identified member of the transforming **growth factor**-.beta. family of regulatory **factors**, also known as **growth differentiation factor 8** (**GDF8**). The nucleotide sequence of human **myostatin** was detd. in 40 individuals. The invariant promoter contains a consensus MyoD binding site, and the coding sequence contains 5 missense substitutions in conserved amino acid residues (A55T, K153R, E164K, P198A, and I225T). Two of these, A55T in exon 1 and K153R in exon 2, are polymorphic in the general population with significantly **different** allele frequencies in Caucasians and African Americans. Neither of the common polymorphisms had a significant impact on muscle mass response to strength training in either Caucasians or African Americans, although skewed allele

frequencies preclude detection of small effects. These allelic variants provide markers for examg. assocn. between the **myostatin** gene and interindividual variation in muscle mass and differences in loss of muscle mass with aging. (c) 1999 Academic Press.

ST **myostatin** gene sequence polymorphism human muscle

IT Genetic element
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(AP-1 site; frequent sequence variation in the human **myostatin** (**GDF8**) gene as a marker for anal. of muscle-related phenotypes)

IT Gene, animal
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(**GDF8**; frequent sequence variation in the human **myostatin** (**GDF8**) gene as a marker for anal. of muscle-related phenotypes)

IT Allele frequency
DNA sequences
Genetic polymorphism
Muscle
Protein sequences
(frequent sequence variation in the human **myostatin** (**GDF8**) gene as a marker for anal. of muscle-related phenotypes)

IT Promoter (genetic element)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(frequent sequence variation in the human **myostatin** (**GDF8**) gene as a marker for anal. of muscle-related phenotypes)

IT Genetic element
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(gene MyoD1 RNA formation factor-responsive element; frequent sequence variation in the human **myostatin** (**GDF8**) gene as a marker for anal. of muscle-related phenotypes)

IT Proteins, specific or class
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(**myostatins**; frequent sequence variation in the human **myostatin/growth-differentiation factor 8** gene as a marker for anal. of muscle-related phenotypes)

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L84 ANSWER 8 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:741730 HCAPLUS
DN 131:321960
TI Anti-**myostatin** vaccine for increasing muscle mass in animals
IN Hickey, Gerard F.
PA Merck and Co., Inc., USA
SO Brit. UK Pat. Appl., 10 pp.
CODEN: BAXXDU
DT Patent
LA English
IC ICM A61K039-395
ICS A61K039-385
ICA C07K014-495
CC 18-6 (Animal Nutrition)
Section cross-reference(s): **15**, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2333706	A1	19990804	GB 1999-2041	19990129 <--
PRAI US 1998-73438P	P	19980202 <--		

AB A method for increasing the muscle mass in animals, such as cow, sheep, pig, and chicken, comprises (a) administering a vaccine which will promote the prodn. of anti-**myostatin** (i.e., anti-**growth differentiation factor 8** or **GDF-8**) antibodies, or (b) providing the animal with an immunoneutralizing amt. of anti-**myostatin** antibodies. **Myostatin**, a member of the transforming **growth factor** (TGF) superfamily of proteins, is thought to exert a neg. control on the amt. of skeletal muscle mass in an animal. The use of a vaccine or antibodies to **myostatin** allows one to increase the skeletal muscle mass in domesticated animals and thus increase their value as food sources. The vaccine may be a hapten-**carrier** protein conjugate in which the hapten is an epitope of **myostatin**, particularly from the functional domain at the C-terminus, or it may be a fusion protein comprising such an epitope fused to a **carrier** protein. The fusion protein product is obtained using std. recombinant DNA procedures using E. coli as host. The vaccine is preferably administered in a formulation also contg. an adjuvant such as an aluminum salt (AlPO4) or an oil-in-water emulsion such as vitamin E acetate solubilizate. Immunoneutralization of **myostatin** may occur after a single dose or a once-yearly dose may be applied. Immunoneutralization may also be induced in pregnant animals resulting in transplacental transfer of anti-**myostatin** antibodies to the fetus and consequent increased muscle mass in the offspring.

ST muscle mass enhancer antibody **myostatin** immunoneutralization
IT Anabolic agents
Muscle
Vaccines
(anti-**myostatin** vaccine for increasing muscle mass in animals)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**myostatin**, antibodies specific for; anti-**myostatin**

vaccine for increasing muscle mass in animals)

IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**myostatin**-specific; anti-**myostatin** vaccine for increasing muscle mass in animals)

IT Meat
(prodn. of; anti-**myostatin** vaccine for increasing muscle mass in animals)

L84 ANSWER 9 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:722919 HCAPLUS
DN 131:332113
TI Methods for treating diabetes by inhibiting **GDF-8**
IN Strassmann, Gideon; Liang, Li-Fang; Topouzis, Stavros
PA Metamorphix, Inc., USA
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-18
ICS A61K039-395
CC 1-10 (Pharmacology)
Section cross-reference(s): 2, **15**
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9956768	A1	19991111	WO 1999-US10089	19990506 <--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9941832	A1	19991123	AU 1999-41832	19990506 <--
	EP 1075272	A1	20010214	EP 1999-925578	19990506 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6368597	B1	20020409	US 1999-305989	19990506 <--
	US 2002031517	A1	20020314	US 2001-988835	20011119 <--
PRAI	US 1998-84490P	P	19980506 <--		
	US 1999-305989	A1	19990506 <--		
	WO 1999-US10089	W	19990506 <--		

AB Methods for treating diabetes by administering an inhibitor of **GDF-8**, or a related member of transforming **growth factor**-.beta. (TGF-.beta.) superfamily of structurally-related **growth factors** (e.g., GDF-11) are disclosed. The **GDF-8** inhibitor is selected from the group consisting of an antibody or antibody fragment, a peptide fragment of **GDF-8**, a dominant-neg. mutant of **GDF-8**, a **GDF-8** receptor antagonist, a non-**GDF-8** peptide, an antisense nucleic acid, and a ribozyme. **GDF-8** inhibition upregulates expression of hexose transporters, such as GLUT4 and GLUT1, and thereby restores insulin sensitivity and reduces systemic glucose levels. Also, the **GDF-8** inhibition upregulates **differentiation** of adipocytes, and thereby increases insulin-sensitive glucose uptake. Thus, interfering with **GDF-8** function could have important applications for the treatment of

type II diabetes, obesity, and disorders related to obesity.

ST **growth differentiation factor 8**
inhibition antidiabetic; antidiabetic **growth factor**
GDF8 inhibition; antiobesity **growth factor**
GDF8 inhibition

IT **Growth factors**, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GDF-11 (**growth/differentiation factor** 11); inhibition of **GDF-8** for treatment of diabetes and related disorders)

IT **Growth factors**, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**GDF-8** (**growth/differentiation factor 8**); inhibition of **GDF-8** for treatment of diabetes and related disorders)

IT Growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**GDF-8**, antagonists; inhibition of **GDF-8** for treatment of diabetes and related disorders)

IT Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**GDF-8**; inhibition of **GDF-8** for treatment of diabetes and related disorders)

IT Transport proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(GLUT-1 (glucose-transporting, 1); upregulation of expression of hexose transporters by **GDF-8** inhibitors in treatment of diabetes)

IT Transport proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(GLUT-4 (glucose-transporting, 4); upregulation of expression of hexose transporters by **GDF-8** inhibitors in treatment of diabetes)

IT Adipose tissue
(adipocyte; inhibition of **GDF-8** for treatment of diabetes and related disorders)

IT Antidiabetic agents
Antiobesity agents
Gene therapy
Hyperglycemia
Muscle
(inhibition of **GDF-8** for treatment of diabetes and related disorders)

IT Antibodies
Antisense DNA
Antisense RNA
Ribozymes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of **GDF-8** for treatment of diabetes and related disorders)

IT Diabetes mellitus
(non-insulin-dependent; inhibition of **GDF-8** for treatment of diabetes and related disorders)

IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.beta.-; inhibition of **GDF-8** or member of TGF-.beta. superfamily for treatment of diabetes and related disorders)

IT 50-99-7, D-Glucose, biological studies 9004-10-8, Insulin, biological

studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(increase of insulin sensitivity and glucose uptake by **GDF-8** inhibitors in treatment of diabetes)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Das, U; Prostaglandins Leukotrienes and Essential Fatty Acids 1999, V60(1), P13 HCAPLUS
(2) John Hopkins University School Of Medicine; WO 9421681 A 1994 HCAPLUS
(3) The John Hopkins University School Of Medicine; WO 9833887 A 1998 HCAPLUS

L84 ANSWER 10 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:549369 HCAPLUS
DN **131:198614**
TI Immunological methods to modulate **myostatin** in vertebrate subjects
IN Barker, Christopher A.; Morsey, Mohamad
PA Biostar Inc., Can.
SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-12
ICS C12N015-62; C12N005-10; C07K014-475; C07K016-22; A61K038-17
CC **15-2** (Immunochemistry)
Section cross-reference(s): 2, 5, 14
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9942573	A1	19990826	WO 1999-CA128	19990219 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6369201	B1	20020409	US 1999-252149	19990218 <--
	ZA 9901369	A	19990820	ZA 1999-1369	19990219 <--
	CA 2323607	AA	19990826	CA 1999-2323607	19990219 <--
	AU 9925073	A1	19990906	AU 1999-25073	19990219 <--
	EP 1056845	A1	20001206	EP 1999-904660	19990219 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9907995	A	20010515	BR 1999-7995	19990219 <--
	JP 2002504326	T2	20020212	JP 2000-532513	19990219 <--
PRAI	US 1998-75213P	P	19980219 <--		
	WO 1999-CA128	W	19990219 <--		

AB Immunol. compns. and methods for reducing **myostatin** activity in vertebrate subjects are disclosed. The compns. include **myostatin** peptide immunogens, **myostatin** multimers and/or **myostatin** immunoconjugates capable of eliciting an immune response in a vertebrate subject to which the compns. are administered. The methods are useful for modulating endogenous **myostatin** activity in vertebrate and are also useful for treating a wide variety of disorders that cause degeneration or wasting of muscle.
ST **myostatin** immunoconjugate vaccine vertebrate muscle degeneration
IT **Immunostimulants**
(adjuvants; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

IT **Epitopes**
Livestock
Molecular cloning
Protein sequences
Vaccines
Vertebrate (Vertebrata)
(compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

IT Antibodies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

IT Muscle, disease
(degeneration; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

IT **Growth factors**, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**growth differentation factor** 11; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

IT T cell (lymphocyte)
(helper cell, epitope; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

IT **Drug delivery systems**
(immunoconjugates; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

IT Appetite
Body weight
Lactation
Longevity
Mammary gland
(increase; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

IT **Toxins**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(leukotoxins, **myostatin** conjugate; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

IT Muscle
(mass and strength increase; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

IT Growth factors, animal
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**myostatin**; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

IT Adipose tissue
(redn.; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

IT Feed
(uptake increase; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous

myostatin and for treating muscle wasting)

IT Muscle, disease
(wasting; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

IT **161135-84-8 161135-86-0 199810-43-0**, **Myostatin** (chicken muscle gene MSTN) **199810-45-2**, **Myostatin** (swine muscle gene MSTN) **240485-48-7**, **Myostatin** (swine) **240485-51-2**, **Myostatin** (sheep) **240485-53-4**, **Myostatin** (chicken) **240485-55-6**, **Myostatin** (turkey) **240485-57-8**, **Myostatin** (zebra fish) **240485-59-0**, 45-376-**Myostatin** (mouse) **240485-61-4**, 45-376-**Myostatin** (rat) **240485-63-6**, 45-375-**Myostatin** (human clone 3) **240485-65-8**, 45-375-**Myostatin** (baboon) **240485-67-0**, 45-375-**Myostatin** (cattle clone 5) **240485-69-2**, 45-375-**Myostatin** (swine) **240485-70-5**, 45-375-**Myostatin** (sheep) **240485-72-7**, 45-375-**Myostatin** (chicken) **240485-73-8**, 45-375-**Myostatin** (turkey) **240485-75-0**, 45-374-**Myostatin** (zebra fish) **240486-08-2**, **Myostatin** (cattle clone 5) **240486-09-3**, 235-376-**Myostatin** (mouse) **240486-14-0**, 235-375-**Myostatin** (human clone 3) **240486-21-9**, 235-375-**Myostatin** (baboon) **240486-26-4**, 235-375-**Myostatin** (cattle clone 5) **240486-35-5**, 235-375-**Myostatin** (sheep) **240486-37-7**, 235-375-**Myostatin** (chicken) **240486-42-4**, 235-375-**Myostatin** (turkey) **240486-46-8**, 235-374-**Myostatin** (zebra fish) **240486-50-4**, 1-350-**Myostatin** (mouse) **240486-52-6**, 1-350-**Myostatin** (rat) **240486-53-7**, 1-350-**Myostatin** (human clone 3) **240486-54-8**, 1-350-**Myostatin** (baboon) **240486-55-9**, 1-350-**Myostatin** (cattle clone 5) **240486-56-0**, 1-350-**Myostatin** (swine) **240486-57-1**, 1-350-**Myostatin** (sheep) **240486-58-2**, 1-350-**Myostatin** (chicken) **240486-59-3**, 1-350-**Myostatin** (turkey) **240486-60-6**, 1-350-**Myostatin** (zebra fish) **240486-61-7**, 1-275-**Myostatin** (mouse) **240486-63-9**, 1-275-**Myostatin** (rat) **240486-64-0**, 1-275-**Myostatin** (human clone 3) **240486-65-1**, 1-275-**Myostatin** (baboon) **240486-66-2**, 1-275-**Myostatin** (cattle clone 5) **240486-67-3**, 1-275-**Myostatin** (swine) **240486-68-4**, 1-275-**Myostatin** (sheep) **240486-69-5**, 1-275-**Myostatin** (chicken) **240486-70-8**, 1-275-**Myostatin** (turkey) **240486-71-9**, 1-275-**Myostatin** (zebra fish) **240486-72-0**, 25-300-**Myostatin** (mouse) **240486-73-1**, 25-300-**Myostatin** (rat) **240486-74-2**, 25-300-**Myostatin** (human clone 3) **240486-76-4**, 25-300-**Myostatin** (baboon) **240486-77-5**, 25-300-**Myostatin** (cattle clone 5) **240486-78-6**, 25-300-**Myostatin** (swine) **240486-79-7**, 25-300-**Myostatin** (sheep) **240486-80-0**, 25-300-**Myostatin** (chicken) **240486-81-1**, 25-300-**Myostatin** (turkey) **240486-82-2**, 25-300-**Myostatin** (zebra fish) **240486-83-3**, 50-325-**Myostatin** (mouse) **240486-90-2**, 50-325-**Myostatin** (rat) **240486-91-3**, 50-325-**Myostatin** (human clone 3) **240486-95-7**, 50-325-**Myostatin** (baboon) **240486-96-8**, 50-325-**Myostatin** (cattle clone 5) **240486-98-0**, 50-325-**Myostatin** (swine) **240486-99-1**, 50-325-**Myostatin** (sheep) **240487-00-7**, 50-325-**Myostatin** (chicken) **240487-01-8**, 50-325-**Myostatin** (turkey)

240487-02-9, 50-325-**Myostatin** (zebra fish)
240487-03-0, 75-350-**Myostatin** (mouse)
240487-04-1, 75-350-**Myostatin** (rat) **240487-05-2**, 75-350-**Myostatin** (human clone 3) **240487-06-3**, 75-350-**Myostatin** (baboon) **240487-07-4**, 75-350-**Myostatin** (cattle clone 5) **240487-08-5**, 75-350-**Myostatin** (swine) **240487-09-6**, 75-350-**Myostatin** (sheep) **240487-10-9**, 75-350-**Myostatin** (chicken) **240487-11-0**, 75-350-**Myostatin** (turkey) **240487-12-1**, 75-350-**Myostatin** (zebra fish) **240487-14-3**, 100-376-**Myostatin** (mouse) **240487-15-4**, 100-376-**Myostatin** (rat) **240487-16-5**, 100-375-**Myostatin** (human clone 3) **240487-17-6**, 100-375-**Myostatin** (baboon) **240487-18-7**, 100-375-**Myostatin** (cattle clone 5) **240487-19-8**, 100-375-**Myostatin** (swine) **240487-20-1**, 100-375-**Myostatin** (sheep) **240487-21-2**, 100-375-**Myostatin** (chicken) **240487-22-3**, 100-375-**Myostatin** (turkey) **240487-23-4**, 100-374-**Myostatin** (zebra fish)
RL: PRP (Properties)
(amino acid sequence; compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

IT 240123-41-5 240123-42-6 240123-43-7 240123-44-8 240123-45-9
240123-46-0 240123-47-1 240123-48-2 240123-49-3 240123-50-6
240123-51-7 240123-52-8 240123-53-9 240123-54-0 240123-55-1
240123-56-2 240123-57-3 240123-58-4 240123-59-5 240123-60-8
240123-61-9 240123-62-0 240123-63-1
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compn. comprising peptide or multimer or immunoconjugate of **myostatin** for modulating endogenous **myostatin** and for treating muscle wasting)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Kambadur; GENOME RESEARCH 1997, V7(9), P910 HCAPLUS
(2) McPherron And Lee; PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA 1997, V94(23), P12457
(3) Michel, G; WO 9902667 A 1999 HCAPLUS
(4) Univ Johns Hopkins Med; WO 9421681 A 1994 HCAPLUS
(5) Univ Johns Hopkins Med; WO 9601845 A 1996 HCAPLUS
(6) Univ Johns Hopkins Med; WO 9833887 A 1998 HCAPLUS

L84 ANSWER 11 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:511238 HCAPLUS
DN 131:125925
TI **Growth differentiation factor-8** from mammalian and avian animals and its role in increasing muscle tissue and bone content
IN Lee, Se-jin; McPherron, Alexandra C.
PA Johns Hopkins University School of Medicine, USA
SO PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N005-00
ICS C12N015-00; C12N015-09; C12N015-63; G01N033-00; A61K039-395; A61K048-00
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 3
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 9940181 A1 19990812 WO 1999-US2511 19990205 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2319703 AA 19990812 CA 1999-2319703 19990205 <--
AU 9925861 A1 19990823 AU 1999-25861 19990205 <--
PRAI US 1998-19070 A 19980205 <--
US 1998-124180 A 19980728 <--
WO 1999-US2511 W 19990205 <--

AB Nucleic acids encoding a novel **growth factor**, designated **growth differentiation factor-8 (GDF-8)**, are provided from 9 mammalian or avian species, which show significant homol. to the known members of the transforming **growth factor**-.beta. superfamily. The predicted **GDF-8** proteins are predicted to contain 2 potential proteolytic processing sites, cleavage of which generates a mature biol. active C-terminal fragment which is capable of forming dimers or heterodimers. The mRNA encoding **GDF-8** is detected almost exclusively in skeletal muscle among a large no. of adult tissues surveyed, and the human gene is located on chromosome 2. A transgenic non-human animal of the species selected from the group consisting of avian, bovine, ovine and porcine having a transgene which results in disrupting the prodn. of and/or activity of **growth differentiation factor-8 (GDF-8)** chromosomally integrated into the germ cells of the animal is disclosed. Also disclosed are methods for making such animals, and methods of treating animals, including humans, with antibodies or antisense directed to **GDF-8**. The animals so treated are characterized by increased muscle tissue and bone content. **GDF-8** has about 92% homol. with GDF-11, and GDF-11 products similar anatomical differences in knockout mice.

ST **growth differentiation factor 8**
cDNA sequence mammal avian; muscle bone content **growth differentiation factor 8**

IT **Growth factors**, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(GDF-11 (**growth differentiation factor 11**); **growth differentiation factor-8** from mammalian and avian animals and its role in increasing muscle tissue and bone content)

IT cDNA sequences
(for **growth differentiation factor-8** from mammalian and avian animals)

IT Baboon
Bone
Cattle
Chicken (Gallus domesticus)
Meat
Mouse
Muscle
Rat
Sheep
Swine
Turkey
(**growth differentiation factor-8** from mammalian and avian animals and its role in increasing muscle tissue and bone content)

IT **Growth factors**, animal
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(**growth differentiation factor-8** from mammalian and avian animals and its role in increasing muscle tissue and bone content)

IT Chromosome
(human 2, human gene located on chromosome 2; **growth differentiation factor-8** from mammalian and avian animals and its role in increasing muscle tissue and bone content)

IT Genetic mapping
(human gene located on chromosome 2; **growth differentiation factor-8** from mammalian and avian animals and its role in increasing muscle tissue and bone content)

IT Gene, animal
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(human gene located on chromosome 2; **growth differentiation factor-8** from mammalian and avian animals and its role in increasing muscle tissue and bone content)

IT Antibodies
Antisense oligonucleotides
RL: AGR (Agricultural use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition or knockout of **GDF-8** by; **growth differentiation factor-8** from mammalian and avian animals and its role in increasing muscle tissue and bone content)

IT Protein sequences
(of **growth differentiation factor-8** from mammalian and avian animals)

IT Kidney, disease
(treatment of; **growth differentiation factor-8** from mammalian and avian animals and its role in increasing muscle tissue and bone content)

IT **161135-84-8 161135-86-0 199810-43-0**,
Myostatin (chicken muscle gene MSTN) **199810-44-1**,
Myostatin (sheep muscle gene MSTN) **199810-45-2**,
Myostatin (swine muscle gene MSTN) **211433-35-1**,
Growth/differentiation factor-8
(baboon) **211433-36-2**, **Growth/differentiation factor-8** (cattle) **211433-38-4**
211433-40-8, **Growth/differentiation factor-8** (turkey)
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(amino acid sequence; **growth differentiation factor-8** from mammalian and avian animals and its role in increasing muscle tissue and bone content)

IT **161135-83-7 161135-85-9 200048-16-4**
200048-19-7 211433-34-0, DNA (baboon **growth/differentiation factor-8** cDNA)
211433-37-3 211433-39-5 211433-41-9
225493-67-4
RL: AGR (Agricultural use); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**;

and adult heart and skeletal muscle, upregulation in cardiomyocytes after infarct, and deletion mutation in heart **myostatin** in Belgian Blue cattle)

IT Heart
(Purkinje fiber; **myostatin** protein and mRNA expression in fetal and adult heart and skeletal muscle, upregulation in cardiomyocytes after infarct, and deletion mutation in heart **myostatin** in Belgian Blue cattle)

IT Transcriptional regulation
(activation; **myostatin** protein and mRNA expression in fetal and adult heart and skeletal muscle, upregulation in cardiomyocytes after infarct, and deletion mutation in heart **myostatin** in Belgian Blue cattle)

IT **Mutation**
(deletion; **myostatin** protein and mRNA expression in fetal and adult heart and skeletal muscle, upregulation in cardiomyocytes after infarct, and deletion mutation in heart **myostatin** in Belgian Blue cattle)

IT Gene
(expression; **myostatin** protein and mRNA expression in fetal and adult heart and skeletal muscle, upregulation in cardiomyocytes after infarct, and deletion mutation in heart **myostatin** in Belgian Blue cattle)

IT Embryo, animal
(fetus; **myostatin** protein and mRNA expression in fetal and adult heart and skeletal muscle, upregulation in cardiomyocytes after infarct, and deletion mutation in heart **myostatin** in Belgian Blue cattle)

IT Protein sequences
(for **myostatin** of Belgian Blue cattle heart)

IT Heart, disease
(infarction; **myostatin** protein and mRNA expression in fetal and adult heart and skeletal muscle, upregulation in cardiomyocytes after infarct, and deletion mutation in heart **myostatin** in Belgian Blue cattle)

IT Heart
(myocyte; **myostatin** protein and mRNA expression in fetal and adult heart and skeletal muscle, upregulation in cardiomyocytes after infarct, and deletion mutation in heart **myostatin** in Belgian Blue cattle)

IT Heart
Muscle
(**myostatin** protein and mRNA expression in fetal and adult heart and skeletal muscle, upregulation in cardiomyocytes after infarct, and deletion mutation in heart **myostatin** in Belgian Blue cattle)

IT mRNA
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**myostatin** protein and mRNA expression in fetal and adult heart and skeletal muscle, upregulation in cardiomyocytes after infarct, and deletion mutation in heart **myostatin** in Belgian Blue cattle)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**myostatin** protein and mRNA expression in fetal and adult heart and skeletal muscle, upregulation in cardiomyocytes after infarct, and deletion mutation in heart **myostatin** in Belgian Blue cattle)

IT Growth factors, animal
RL: ADV (Adverse effect, including toxicity); BPR (Biological process);

BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**myostatin**; **myostatin** protein and mRNA expression in fetal and adult heart and skeletal muscle, upregulation in cardiomyocytes after infarct, and deletion mutation in heart **myostatin** in Belgian Blue cattle)
IT cDNA sequences
(of **myostatin** of Belgian Blue cattle heart)
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Birdsall, H; Circulation 1997, V95, P684 HCAPLUS
(2) Boccard, R; Developments in meat science 1981, V2, P1
(3) Brand, T; J Mol Cell Cardiol 1995, V27, P5 HCAPLUS
(4) Engelmann, G; Mech Dev 1992, V38, P85 HCAPLUS
(5) Grobet, L; Nat Genet 1997, V1, P71
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(8) Kambadur, R; Genome Res 1997, V7, P910 HCAPLUS
(9) Kingsley, D; Genes Dev 1994, V8, P133 HCAPLUS
(10) MacLellan, W; Circ Res 1993, V73, P783 HCAPLUS
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(12) McPherron, A; Nature 1997, V387, P83 HCAPLUS
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(14) Millan, F; Development 1991, V111, P131 HCAPLUS
(15) Pelton, R; J Cell Biol 1991, V115, P1091 HCAPLUS
(16) Pott, J; Proc Natl Acad Sci USA 1991, V88, P1516
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(22) Wu, C; Transplantation 1992, V54, P326 MEDLINE

L84 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:113811 HCAPLUS
DN 130:163590
TI Methods of cloning genes for animal **growth/differentiation factor** receptors
IN Lee, Se-Jin; McPherron, Alexandra
PA The Johns Hopkins University School of Medicine, USA
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-12
ICS G01N033-53
CC 2-1 (Mammalian Hormones)
Section cross-reference(s): 1, 3
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9906559	A1	19990211	WO 1998-US15598	19980728	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	AU 9886663	A1	19990222	AU 1998-86663	19980728	<--
PRAI	US 1997-54461P	P	19970801	<--		

WO 1998-US15598 W 19980728 <--

AB Receptors for the **growth differentiation factor (GDF)** family of **growth factors** and methods of identifying such receptors are described. Also included are methods of identifying antibodies to the receptors, receptor fragments that inhibit **GDF** binding, and **GDF** receptor-binding agents capable of blocking **GDF** binding to the receptor. The receptors of the invention allow the identification of antagonists or agonists useful for agricultural and human therapeutic purposes.

ST **growth differentiation factor** receptor gene cloning; antibody **growth differentiation factor** receptor; effector **growth differentiation factor** screening receptor gene cloning

IT Peptidomimetics
(as effectors of **growth differentiation factors**; methods of cloning genes for animal **growth/differentiation factor** receptors)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as effectors of **growth differentiation factors**; methods of cloning genes for animal **growth/differentiation factor** receptors)

IT Development, mammalian postnatal
(effects of **GDF**-11 knockout mutation on; methods of cloning genes for animal **growth/differentiation factor** receptors)

IT Drug screening
(for effectors of **growth differentiation factors**; methods of cloning genes for animal **growth/differentiation factor** receptors)

IT Retroviral vectors
(for expression of **growth differentiation factor** genes in transgenic animals; methods of cloning genes for animal **growth/differentiation factor** receptors)

IT Antisense DNA
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for inhibition of expression of **growth differentiation factor** genes; methods of cloning genes for animal **growth/differentiation factor** receptors)

IT **Growth factors**, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**growth/differentiation factor** 11, receptors for; methods of cloning genes for animal **growth/differentiation factor** receptors)

IT Receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(**growth/differentiation factor** 11; methods of cloning genes for animal **growth/differentiation factor** receptors)

IT **Growth factors**, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**growth/differentiation factor 8**, receptors for; methods of cloning genes for animal **growth/differentiation factor** receptors)

IT Receptors

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(**growth/differentiation factor 8**
; methods of cloning genes for animal **growth/differentiation factor** receptors)
IT **Mutation**
(knockout, of mouse **growth/differentiation factor** 11 gene, phenotype of; methods of cloning genes for animal **growth/differentiation factor** receptors)
IT Antibodies
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, to **growth/differentiation factor** receptors; methods of cloning genes for animal **growth/differentiation factor** receptors)
IT Molecular cloning
(of genes for **growth/differentiation factor** receptors; methods of cloning genes for animal **growth/differentiation factor** receptors)
IT Genetic engineering
(of responsiveness to **growth/differentiation factors**; methods of cloning genes for animal **growth/differentiation factor** receptors)
IT **Growth factors**, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptors for; methods of cloning genes for animal **growth/differentiation factor** receptors)
IT Antibodies
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to **growth/differentiation factor** receptors; methods of cloning genes for animal **growth/differentiation factor** receptors)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bouizar, Z; European Journal of Biochemistry 1986, V155, P141 HCAPLUS
(2) Hannon, K; Journal of Cellular Biochemistry 1996, V132(6), P1151 HCAPLUS
(3) McPherron, A; Nature 1997, V387(6628), P83 HCAPLUS
(4) Wozney; US 5639638 A 1997 HCAPLUS

L84 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:64915 HCAPLUS
DN **130:134990**
TI Mutations in the **myostatin** gene cause double-muscling in mammals
IN Grobet, Luc; Georges, Michel; Poncelet, Dominique
PA University of Liege, Belg.
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-00
ICS C12N015-12; C07K014-495; C12N005-10; C12Q001-68; A01K067-027; A61K048-00
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 6, 13, 14, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9902667	A1	19990121	WO 1998-IB1197	19980714 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	US 6103466	A	20000815	US 1997-891789	19970714	<--
	AU 9884571	A1	19990208	AU 1998-84571	19980714	<--
	EP 1002068	A1	20000524	EP 1998-935228	19980714	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 2001509378	T2	20010724	JP 2000-502165	19980714	<--
PRAI	US 1997-891789	A2	19970714	<--		
	US 1998-7761	A2	19980115	<--		
	WO 1998-IB1197	W	19980714	<--		

AB Genes (cDNA) encoding bovine and human **myostatin** proteins are provided contg. open reading frames encoding proteins of 375 amino acids in length. A mutant gene in which the coding sequence lacks an 11-bp consecutive sequence of the sequence encoding bovine protein having **myostatin** activity was sequenced. Cattle of the Belgian Blue breed homozygous for the mutant gene lacking **myostatin** activity are double-muscled. A method for detg. the presence of muscular hyperplasia in a mammal is described. The method includes obtaining a sample of material contg. DNA from the mammal and ascertaining whether a sequence of the DNA encoding (a) a protein having biol. activity of **myostatin**, is present, and whether a sequence of the DNA encoding (b) an allelic protein lacking the activity of (a), is present. The absence of (a) and the presence of (b) indicates the presence of muscular hyperplasia in the mammal.

ST **myostatin** gene sequence mutation muscular hyperplasia; bovine **myostatin** gene mutation muscular hyperplasia; human **myostatin** gene mutation muscular hyperplasia

IT PCR (polymerase chain reaction)
(RT-PCR (reverse transcription-PCR), primers for diagnostic kit; mutations in the **myostatin** gene cause double-muscling in mammals)

IT cDNA sequences
(for **myostatin** from bovine and human)

IT Diagnosis
(genetic; mutations in the **myostatin** gene cause double-muscling in mammals)

IT Ribozymes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(increasing muscle mass by treatment with; mutations in the **myostatin** gene cause double-muscling in mammals)

IT Muscle, disease
(muscular hyperplasia; mutations in the **myostatin** gene cause double-muscling in mammals)

IT Cattle
Genetic mapping
Molecular cloning
Mutation
Test kits
(mutations in the **myostatin** gene cause double-muscling in mammals)

IT Gene, animal
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(mutations in the **myostatin** gene cause double-muscling in mammals)

IT Primers (nucleic acid)
Probes (nucleic acid)
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical

study); BIOL (Biological study); USES (Uses)
(mutations in the **myostatin** gene cause double-muscling in mammals)
IT Proteins, specific or class
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**myostatins**; mutations in the **myostatin** gene cause double-muscling in mammals)
IT Protein sequences
(of **myostatin** from bovine and human)
IT DNA sequences
(of **myostatin** gene from bovine)
IT Genetic mapping
(phys.; mutations in the **myostatin** gene cause double-muscling in mammals)
IT 219991-75-0 219991-76-1
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(PCR primer; mutations in the **myostatin** gene cause double-muscling in mammals)
IT **161135-86-0 219991-53-4**, **Myostatin** (cattle)
219991-78-3
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); PRP (Properties); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; mutations in the **myostatin** gene cause double-muscling in mammals)
IT **219991-52-3**, DNA (cattle **myostatin** cDNA plus flanks)
219991-54-5, DNA (human **myostatin** cDNA plus flanks)
219991-68-1, DNA (cattle **myostatin** gene plus flanks)
219991-77-2
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); PRP (Properties); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleotide sequence; mutations in the **myostatin** gene cause double-muscling in mammals)
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Charlier; Mammalian Genome 1995, V6(11), P788 HCAPLUS
(2) Dickman; Science 1997, V277(5334), P1922 HCAPLUS
(3) Georges; Genome Research 1996, V6, P907 HCAPLUS
(4) Grobet; Mamm Genome 1998, V9(3), P210 HCAPLUS
(5) Grobet; Nature Genetics 1997, V17(1), P71 HCAPLUS
(6) Kambadur; Genome Research 1997, V7(9), P910 HCAPLUS
(7) Kappes; Genome Research 1997, V7, P235 HCAPLUS
(8) McPherron; Nature 1997, V387, P83 HCAPLUS
(9) McPherron; Proc Natl Acad Sci USA 1997, V94(23), P12457 HCAPLUS
(10) Smith; Mammalian Genome 1997, V8(10), P742 HCAPLUS
(11) Univ Johns Hopkins Med; WO 9421681 A 1994 HCAPLUS
(12) Univ Johns Hopkins Med; WO 9833887 A 1998 HCAPLUS
(13) Westhusin, M; Nature Genetics 1997, V17(1), P4 HCAPLUS
(14) Westhusin, M; Nature Genetics 1997, V17(1), P71

L84 ANSWER 15 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:543145 HCAPLUS
DN 129:170982
TI Transgenic animals with disrupted expression of **growth differentiation factor-8** or animals administered with antibodies to **GDF-8**
IN Lee, Se-Jin; McPherron, Alexandra C.
PA The Johns Hopkins University School of Medicine, USA
SO PCT Int. Appl., 125 pp.

CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N005-00
ICS C12N015-00; C12N015-09; C12N015-63
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 1, 3, **15**, 17
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9833887	A1	19980806	WO 1998-US2479	19980205 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5994618	A	19991130	US 1997-795071	19970205 <--
	AU 9862742	A1	19980825	AU 1998-62742	19980205 <--
PRAI	US 1997-795071		19970205 <--		
	US 1997-847910		19970428 <--		
	US 1997-862445		19970523 <--		
	WO 1998-US2479		19980205 <--		

AB Disclosed is a transgenic non-human animal having a transgene encoding antisense polynucleotides to disrupt the prodn. of **growth differentiation factor-8** (**GDF-8**), which animal exhibits increased muscle mass or decreased cholesterol content. The goal may also be achieved by administering domestic animals with (monoclonal) antibodies to **GDF-8**. Also disclosed are the cDNA sequences encoding **GDF-8** from rat, mouse, human, chicken, baboon, turkey, and cattle, and their deduced amino acid sequences. Also described is a gene therapy method involved with interrupting the expression of **growth differentiation factor-8** for treating a variety of muscle diseases, AIDS, cachechia, etc.

ST cDNA sequence **growth differentiation factor 8**; muscle increment transgenic animal; cholesterol redn transgenic animal; antibody **growth differentiation factor 8**; antisense **growth differentiation factor 8**

IT Antiobesity agents
Antitumor agents
(antisense oligonucleotide of or antibodies to **growth differentiation factor-8** for)
IT AIDS (disease)
Aging, animal
Muscular dystrophy
Neuromuscular diseases
(antisense oligonucleotide of or antibodies to **growth differentiation factor-8** for treatment of)
IT Muscle, disease
(atrophy; antisense oligonucleotide of or antibodies to **growth differentiation factor-8** for treatment of)
IT Meat
(beef; transgenic animals with disrupted expression of **growth differentiation factor-8** for prodn. of)
IT Egg, poultry
(cholesterol-low; transgenic animals with disrupted expression of **growth differentiation factor-8** or animals administered with antibodies to **GDF-8**)
IT **Growth factors**, animal

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**growth differentiation factor-8**
; transgenic animals with disrupted expression of **growth differentiation factor-8** or animals administered with antibodies to **GDF-8**)

IT Spinal cord
(injury; antisense oligonucleotide of or antibodies to **growth differentiation factor-8** for treatment of)

IT Meat
(lamb; transgenic animals with disrupted expression of **growth differentiation factor-8** for prodn. of)

IT Antibodies
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal, to **growth differentiation factor-8**; transgenic animals with disrupted expression of **growth differentiation factor-8** low in)

IT Lung, disease
(obstructive; antisense oligonucleotide of or antibodies to **growth differentiation factor-8** for treatment of)

IT cDNA sequences
(of cDNA for **growth differentiation factor-8** of animals)

IT Protein sequences
(of **growth differentiation factor-8** of animals)

IT Meat
(pork; transgenic animals with disrupted expression of **growth differentiation factor-8** for prodn. of)

IT Antibodies
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(to **growth differentiation factor-8**; transgenic animals with disrupted expression of **growth differentiation factor-8** low in)

IT Antisense oligonucleotides
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(transgenic animals with disrupted expression of **growth differentiation factor-8**)

IT Milk
(transgenic animals with disrupted expression of **growth differentiation factor-8** for prodn. of)

IT Muscle
(transgenic animals with disrupted expression of **growth differentiation factor-8** high in)

IT Animal
Baboon
Chicken (Gallus domesticus)
Molecular cloning
Rat
Turkey
(transgenic animals with disrupted expression of **growth differentiation factor-8** or animals administered with antibodies to **GDF-8**)

IT Gene, animal
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); USES (Uses)

(transgenic animals with disrupted expression of **growth differentiation factor-8** or animals administered with antibodies to **GDF-8**)

IT Bird (Aves)
Cattle
Fish
Mouse
Sheep
Swine
(transgenic; transgenic animals with disrupted expression of **growth differentiation factor-8** or animals administered with antibodies to **GDF-8**)

IT Injury
(trauma; antisense oligonucleotide of or antibodies to **growth differentiation factor-8** for treatment of)

IT Muscle, disease
(wasting; antisense oligonucleotide of or antibodies to **growth differentiation factor-8** for treatment of)

IT **199810-43-0, Myostatin** (chicken muscle gene MSTN)
211433-35-1, Growth/differentiation factor-8 (baboon) **211433-36-2, Growth /differentiation factor-8** (cattle)
211433-38-4
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; transgenic animals with disrupted expression of **growth differentiation factor-8** or animals administered with antibodies to **GDF-8**)

IT **211433-40-8, Growth/differentiation factor-8** (turkey)
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; transgenic animals with disrupted expression of **growth differentiation factor-8** or animals administered with antibodies to **GDF-8**)

IT **161135-84-8 200048-19-7 211433-34-0 211433-37-3 211433-39-5 211433-41-9**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(nucleotide sequence; transgenic animals with disrupted expression of **growth differentiation factor-8** or animals administered with antibodies to **GDF-8**)

IT 57-88-5, Cholesterol, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(transgenic animals with disrupted expression of **growth differentiation factor-8** low in)

IT **161135-83-7 161135-86-0**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(transgenic animals with disrupted expression of **growth differentiation factor-8** or animals administered with antibodies to **GDF-8**)

IT **161135-85-9**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(transgenic animals with disrupted expression of **growth differentiation factor-8** or animals administered with antibodies to **GDF-8**)

L84 ANSWER 16 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:768637 HCAPLUS

DN 128:57742
TI Double muscling in cattle due to mutations in the **myostatin** gene
AU Mcpherron, Alexandra C.; Lee, Se-Jin
CS Department of Molecular Biology and Genetics, Johns Hopkins University School of Medicine, Baltimore, MD, 21205, USA
SO Proceedings of the National Academy of Sciences of the United States of America (**1997**), 94(23), 12457-12461
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 3, 12, 14
AB **Myostatin** (**GDF-8**) is a member of the transforming **growth factor** .beta. superfamily of secreted **growth** and **differentiation factors** that is essential for proper regulation of skeletal muscle mass in mice. Here the authors report the **myostatin** sequences of nine other vertebrate species and the identification of mutations in the coding sequence of bovine **myostatin** in two breeds of double-muscled cattle, Belgian Blue and Piedmontese, which are known to have an increase in muscle mass relative to conventional cattle. The Belgian Blue **myostatin** sequence contains an 11-nucleotide deletion in the third exon which causes a frameshift that eliminates virtually all of the mature, active region of the mol. The Piedmontese **myostatin** sequence contains a missense mutation in exon 3, resulting in a substitution of tyrosine for an invariant cysteine in the mature region of the protein. The similarity in pheno-types of double-muscled cattle and **myostatin** null mice suggests that **myostatin** performs the same biol. function in these two species and is a potentially useful target for genetic manipulation in other farm animals.
ST vertebrate DNA protein sequence **myostatin**; muscling cattle **myostatin** gene mutation
IT Cattle
(Belgian Blue and Piedmontese; double muscling in cattle due to mutations in **myostatin** gene)
IT Gene, animal
RL: PRP (Properties)
(MSTN; double muscling in cattle due to mutations in **myostatin** gene)
IT **Mutation**
(deletion; double muscling in cattle due to mutations in **myostatin** gene)
IT Cell differentiation
Chicken (Gallus domesticus)
Danio rerio
Papio hamadryas
Protein sequences
Rat (Rattus norvegicus)
Sheep
Swine
Turkey
Vertebrate (Vertebrata)
cDNA sequences
(double muscling in cattle due to mutations in **myostatin** gene)
IT Muscle
(doubling; double muscling in cattle due to mutations in **myostatin** gene)
IT **Mutation**
(frameshift; double muscling in cattle due to mutations in **myostatin** gene)
IT Protein sequences

(homol.; double muscling in cattle due to mutations in **myostatin** gene)
IT Evolution
(mol.; double muscling in cattle due to mutations in **myostatin** gene)
IT Growth factors, animal
RL: PRP (Properties)
(**myostatins**; double muscling in cattle due to mutations in **myostatin** gene)
IT **Mutation**
(nonsense; double muscling in cattle due to mutations in **myostatin** gene)
IT **Mutation**
(substitution; double muscling in cattle due to mutations in **myostatin** gene)
IT **Mutation**
(transition; double muscling in cattle due to mutations in **myostatin** gene)
IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.beta.-; double muscling in cattle due to mutations in **myostatin** gene)
IT **161135-86-0, Growth/differentiation factor 8** (human) **199810-41-8**
199810-42-9, Myostatin (cattle muscle gene MSTN)
199810-43-0, Myostatin (chicken muscle gene MSTN)
199810-44-1, Myostatin (sheep muscle gene MSTN)
199810-45-2, Myostatin (swine muscle gene MSTN)
199810-46-3 199810-47-4, Myostatin (turkey muscle gene MSTN) **199810-48-5, Myostatin** (Danio rerio muscle gene MSTN)
RL: PRP (Properties)
(amino acid sequence; double muscling in cattle due to mutations in **myostatin** gene)
IT **200048-13-1**, GenBank AF019619 **200048-14-2**, GenBank AF019620 **200048-15-3**, GenBank AF019621 **200048-16-4**, GenBank AF019622 **200048-17-5**, GenBank AF019623 **200048-18-6**, GenBank AF019624 **200048-19-7**, GenBank AF019625 **200048-20-0**, GenBank AF019626 **200048-21-1**, GenBank AF019627
RL: PRP (Properties)
(nucleotide sequence; double muscling in cattle due to mutations in **myostatin** gene)

L84 ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:529757 HCAPLUS
DN 127:229679
TI Growth control: action mouse
AU Slack, J. M. W.
CS Dep. Biol. Biochem., Univ. Bath, Bath, BA2 7AY, UK
SO Curr. Biol. (**1997**), 7(8), R467-R469
CODEN: CUBLE2; ISSN: 0960-9822
PB Current Biology
DT Journal; General Review
LA English
CC 2-0 (Mammalian Hormones)
AB A review, with 11 refs. A recently described knockout mouse has abnormally large muscles. The phenotype suggests that the ablated product, **growth differentiation factor 8** or **myostatin**, may be 1 of the long sought inhibitors that control the **growth** of individual tissues and organs.
ST review mouse growth **myostatin**
IT **Growth factors** (animal)

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(**growth differentiation factor-8**
; **myostatin** in **growth** control in mice)
IT Growth (animal)
Mouse
(**myostatin** in growth control in mice)

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MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

=> d all

L121 ANSWER 1 OF 1 MEDLINE
AN 2000079152 MEDLINE
DN **20079152** PubMed ID: **10610713**
TI Frequent sequence variation in the human myostatin (**GDF8**) gene as a marker for analysis of muscle-related phenotypes.
AU Ferrell R E; Conte V; Lawrence E C; Roth S M; Hagberg J M; Hurley B F
CS Department of Human Genetics, Graduate School of Public Health, Pittsburgh, Pennsylvania 15261, USA.. rferrell@helix.hgen.pitt.edu
NC AG15389 (NIA)
AG16205 (NIA)
DK46204 (NIDDK)
SO GENOMICS, **(1999 Dec 1)** 62 (2) 203-7.
Journal code: 8800135. ISSN: 0888-7543.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200002
ED Entered STN: 20000218
Last Updated on STN: 20020212
Entered Medline: 20000209
AB Myostatin is a recently identified member of the transforming **growth factor**-beta family of regulatory **factors**, also known as **growth** and **differentiation factor 8** (**GDF8**). The nucleotide sequence of human myostatin was determined in 40 individuals. The invariant promoter contains a consensus MyoD binding site, and the coding sequence contains five missense substitutions in conserved amino acid residues (A55T, K153R,

E164K, P198A, and I225T). Two of these, A55T in exon 1 and K153R in exon 2, are polymorphic in the general population with significantly different allele frequencies in Caucasians and African Americans ($P < 0.001$). Neither of the common polymorphisms had a significant impact on muscle mass response to strength training in either Caucasians or African Americans, although skewed allele frequencies preclude detection of small effects. These allelic variants provide markers for examining association between the myostatin gene and interindividual variation in muscle mass and differences in loss of muscle mass with aging.

CT Check Tags: Animal; Female; Human; Male; Support, U.S. Gov't, P.H.S.
Amino Acid Substitution: GE, genetics
Asian Americans: GE, genetics
Base Sequence
Caucasoid Race: GE, genetics
Exercise: PH, physiology
Genetic Markers
Molecular Sequence Data
Muscle Development
Muscle, Skeletal: GD, growth & development
*Muscle, Skeletal: PH, physiology
Negroid Race: GE, genetics
Phenotype
Promoter Regions (Genetics)
*Transforming Growth Factor beta: GE, genetics
*Variation (Genetics)
CN 0 (Genetic Markers); 0 (Transforming Growth Factor beta); 0 (myostatin)

=> fil wpix
FILE 'WPIX' ENTERED AT 15:26:18 ON 03 JUN 2002

FILE LAST UPDATED: 28 MAY 2002 <20020528/UP>
MOST RECENT DERWENT UPDATE 200234 <200234/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> The BATCH option for structure searches has been enabled in WPINDEX/WPIDS and WPIX >>>

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

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>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT: http://www.derwent.com/userguides/dwpi_guide.html <<<

=> d all abeq tech tot

L132 ANSWER 1 OF 4 WPIX (C) 2002 THOMSON DERWENT
AN 2001-112680 [12] WPIX
DNC **C2001-033610**
TI Increasing the muscle mass of animals used in meat production by down regulating **growth differentiation factor 8** (**GDF-8**) activity in the animal through induction of anti-**GDF-8** antibody production.
DC B04 C06 D16

IN HALKIER, T; KLYSNER, S; MOURITSEN, S
PA (MEBI-N) M & E BIOTECH AS; (PHAR-N) PHARMEXA AS
CYC 94
PI WO 2001005820 A2 20010125 (200112)* EN 110p C07K014-00 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000059675 A 20010205 (200128) C07K014-00 <--
NO 2001006252 A 20020315 (200232) C07K000-00 <--
ADT WO 2001005820 A2 WO 2000-DK413 20000720; AU 2000059675 A AU 2000-59675 20000720; NO 2001006252 A WO 2000-DK413 20000720, NO 2001-6252 20011219
FDT AU 2000059675 A Based on WO 200105820
PRAI US 1999-145275P 19990726; DK 1999-1014 19990720
IC ICM **C07K000-00; C07K014-00**
AB WO 200105820 A UPAB: 20010302
NOVELTY - In vivo down regulation of **growth differentiation factor 8** (**GDF-8**) activity in an animal, including a human, comprises presentation of a **GDF-8** polypeptide or subsequence or **GDF-8** analogue with a modified amino acid sequence to the immune system of the animal which induces production of anti-**GDF-8** antibodies.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a **GDF-8** analogue derived from an animal **GDF-8** polypeptide which has a modification so that it induces production of anti-**GDF-8** antibodies when used to immunize an animal;

(2) a nucleic acid (I) encoding the **GDF-8** analogue of (1);

(3) a vector carrying (I) capable of autonomous replication;

(4) a transformed cell carrying the vector of (3) capable of replicating (I);

(5) a stable cell line carrying the vector of (3) that expresses (I) and optionally secretes on carries the **GDF-8** analogue on its surface;

(6) preparation of the cell of (4);

(7) method for identifying a modified **GDF-8** polypeptide capable of inducing antibodies against unmodified **GDF-8** (self-protein) in an animal comprising preparing a set of mutually distinct modified **GDF-8** polypeptides which have amino acid (aa) insertions, deletions or substitutions giving aa sequences containing foreign T-cell epitopes, testing members of the set for their ability to induce production of antibodies by the animal against unmodified **GDF-8** and isolating members of the set which are able to induce this antibody production; and

(8) method for preparing an immunogenic composition which contains at least one modified **GDF-8** polypeptide capable of inducing antibodies against unmodified **GDF-8** (self-protein) in an animal.

ACTIVITY - Cardiant; immunomodulator.

No biological data is given.

MECHANISM OF ACTION - Vaccine.

USE - Down-regulation of **GDF-8** activity is used to increase muscle mass in animals at least 5% when compared with animals with normal **GDF-8** activity and up to at least 45% (claimed).

The method increases muscle mass in animals such as cows, pigs and poultry which are used for meat production. The down-regulation of **GDF-8** activity is used to stimulate **growth** of

skeletal muscle mass in animals. Anti-**GDF8** vaccines can be used to treat human diseases such as cancer cachexia where muscle atrophy is pronounced and for patients suffering from acute and chronic heart failure.

ADVANTAGE - Using this method to increase muscle mass removes the need for extensive use of antibiotics in farm animals which can induce cross resistance towards human antibiotics in microorganisms pathogenic in man. Antibiotics only obtain a low **growth** rate but up to at least 45% increase in muscle mass is achieved with the new method. **Growth** hormones have also been used in the prior art but these are expensive and have the potential of the presence of residual hormones in meat. The treatment can be reserved for animals which are predestined for slaughter. The treatment should only require 1-4 annual injections but using **growth** hormones and antibiotics required more frequent administration.

Dwg.0/5

FS CPI

FA AB; DCN

MC CPI: B04-E02B; B04-E03B; B04-E08; B04-F0200E; B04-F0700E; B04-F0800E; B04-F0900E; B04-F10A3E; B04-F10A8E; B04-F10B1E; B04-F10B2E; B04-F1100E; B04-G02; B04-H06; B04-H0600E; B11-C07A; B12-K04A; B14-F01B; B14-G03; B14-J05; B14-S11; C04-E02B; C04-E03B; C04-E08; C04-F0200E; C04-F0700E; C04-F0800E; C04-F0900E; C04-F10A3E; C04-F10A8E; C04-F10B1E; C04-F10B2E; C04-F1100E; C04-G02; C04-H06; C04-H0600E; C11-C07A; C12-K04A; C14-J05; C14-S11; D05-H09; D05-H11; D05-H12A; D05-H12B2; D05-H12E; D05-H14A1; D05-H14A2; D05-H14B1; D05-H14B2; D05-H14B3; D05-H17A2

TECH UPTX: 20010302

TECHNOLOGY FOCUS - BIOLOGY - Preferred Polypeptide: The **GDF-8** subsequence or **GDF-8** analogue is derived from the C-terminal, active form of **GDF-8** e.g. from a bovine, porcine, human, chicken, sheep or turkey **GDF-8**.

The **GDF-8** polypeptide is modified by a substitution of at least one aa sequence in the two polypeptide sequences of 109 aa given in the specification with at least one aa sequence of an equal or different length which contains a foreign TH epitope. The substituted residues are preferably 1-12, 18-41, 43-48, 49-69 or 74-104 in the 109 aa sequences. Alternatively the modification is an insertion of a foreign TH epitope sequence where the insertion occurs anywhere in positions 1-12, 18-30, 42-51, 82-86 or 105-109 in the 109 aa sequences.

The analogue of **GDF-8** has at least one modification of the aa sequence which is substitution, deletion, insertion and/or addition but preserves the overall tertiary structure of **GDF-8**.

The **GDF-8** modification:

(1) preserves a substantial fraction of **GDF-8** B-cell epitopes; and

(2) introduces at least one foreign T helper lymphocyte (TH) epitope and/or functional groups; and/or

(3) introduces at least one first functional group which effects targeting of the modified molecule to an antigen presenting cell (APC) or a B-lymphocyte; and/or

(4) introduces at least one second functional group which stimulates the immune system; and/or

(5) introduces at least one third functional group which optimizes presentation of the modified **GDF-8** to the immune system.

The first functional group is a substantially specific binding partner for a B-lymphocyte or APC specific surface antigen e.g. a hapten or carbohydrate which has a receptor on the B-lymphocyte or APC, e.g. mannose or mannan.

The second functional group is a cytokine, hormone or heat shock protein (HSP) e.g. interferon-gamma (IFN-gamma), Flt3L, interleukin (IL) 1, IL-2,

IL-3, IL-6, IL-12, IL-13, IL-15, granulocyte-macrophage colony stimulating factor (GM-CSF), HSP70, HSP90, HSC70, GRP94 or calreticulin (CRT).
The third functional group is a lipid e.g. palmitoyl, myristyl, farnesyl, geranyl-geranyl, N-acyl diglyceride group or a GPI-anchor.
The modification is an introduction by covalent or non-covalent binding to suitable chemical groups in **GDF-8** or subsequence of the foreign TH epitope or functional groups as side groups. The modification can provide a fusion polypeptide. The modification includes duplication of at least one **GDF-8** B-cell epitope and/or introduction of a hapten. The foreign T cell epitope is immunodominant in the animal, is promiscuous, such as a natural promiscuous T cell epitope (e.g. Tetanus toxoid epitope P2 or P30 or a diphtheria toxoid epitope, an influenza virus hemagglutinin epitope and a P. falciparum CS epitope), and an artificial major histocompatibility (MHC)-II binding peptide sequence.
Preferred Method: At least two copies of the **GDF-8** polypeptide, subsequence or modified **GDF-8** covalently or non-covalently linked to a carrier molecule are presented to the immune system.
Nucleic acids (naked DNA, DNA formulated with optionally charged lipids, in liposomes, with transfection facilitating or targeting protein or polypeptide, with calcium precipitating agents, with chitin or chitosan, with an adjuvant DNA in a viral vector or DNA coupled to an inert carrier molecule) encoding the modified **GDF-8** are introduced into the animal cells to obtain in vivo expression of the nucleic acids introduced. The nucleic acids are formulated in a virtual lymph node device. A non-pathogenic microorganism (Escherichia coli, Bacillus, Salmonella, Mycobacterium bovis BCG) or virus (non-virulent pox e.g. vaccinia) carrying nucleic acid fragment encoding the **GDF-8** polypeptide or analogue is administered once to the animal.
Preferred Vector: The vector is a plasmid, phage, cosmid, minichromosome or a virus. The vector comprises in the 5' to 3' direction and in operable linkage a promoter for driving expression of (I), optionally a nucleic acid sequence encoding a leader peptide enabling secretion or integration into the membrane of the polypeptide, (I) and optionally a terminator. The vector is optionally capable of being integrated into the genome of the hosts cell. The promoter drives expression in a prokaryotic or eukaryotic cell.
Preferred Cell: The transformed cell is a microorganism e.g. Escherichia coli, Bacillus, Salmonella, Mycobacterium bovis BCG, yeast, protozoan, fungus, insect e.g. S2 or SF cell, plant or mammalian cell. The transformed cell secretes or carries the **GDF-8** analogue on its surface.
Preparation: The cell is prepared by transforming a host cell with (I) or a vector carrying (I) (claimed). The immunogenic composition is prepared by:
(1) preparing by peptide synthesis or genetic engineering a set of mutually distinct modified **GDF-8** polypeptides which have aa insertions, deletions or substitutions giving aa sequences containing foreign T-cell epitopes;
(2) testing members of the set for their ability to induce production of antibodies by the animal against unmodified **GDF-8**; and
(3) admixing the member(s) of the set which are able to induce this antibody production with a carrier and/or vehicle and optionally with an adjuvant.
The set of mutually distinct modified **GDF-8** polypeptides can be prepared by inserting (I) into an expression vector which is transformed into suitable host cells and then expressing (I) and isolating the expression products.

L132 ANSWER 2 OF 4 WPIX (C) 2002 THOMSON DERWENT
AN 2000-505849 [45] WPIX
DNN **N2000-374068** DNC **C2000-151829**

TI Novel method for identifying inhibitors of **growth differentiation factor** (**GDF**) proteins which used to treat a variety of diseases.

DC B04 C06 D16 P14 S03

IN BRADY, J L; LIANG, L; RATOVITSKI, T; SINHA, D; TOPOUZIS, S; WRIGHT, J F; YASWEN-CORKERY, L

PA (META-N) METAMORPHIX INC

CYC 91

PI WO 2000043781 A2 20000727 (200045)* EN 122p G01N033-50
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000025140 A 20000807 (200055) G01N033-50
EP 1147413 A2 20011024 (200171) EN G01N033-50
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
BR 2000008188 A 20020213 (200220) G01N033-50

ADT WO 2000043781 A2 WO 2000-US1552 20000121; AU 2000025140 A AU 2000-25140 20000121; EP 1147413 A2 EP 2000-903387 20000121, WO 2000-US1552 20000121; BR 2000008188 A BR 2000-8188 20000121, WO 2000-US1552 20000121

FDT AU 2000025140 A Based on WO 200043781; EP 1147413 A2 Based on WO 200043781; BR 2000008188 A Based on WO 200043781

PRAI US 1999-138363P 19990610; US 1999-116639P 19990121

IC ICM G01N033-50
ICS A01K067-027; **C07K007-06**; **C07K007-08**; **C07K014-475**; **C07K014-51**; C12N009-00; C12N015-11; G01N033-68

AB WO 200043781 A UPAB: 20000918
NOVELTY - Identifying an inhibitor (I) of a **GDF** protein comprises obtaining medium in which cells producing a **GDF** protein have been cultured, and testing the medium for the ability to inhibit **GDF** activity.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method of identifying (I), comprising preparing fragments of a **GDF** protein, and testing the fragments for the ability to inhibit **GDF** activity;

(2) a **GDF**-8 or **GDF**-11 inhibitor which can be isolated from medium in which CHO cells stably transfected with an expression plasmid containing an insert encoding human **GDF**-8 or **GDF**-11 have been isolated by ion exchange chromatography, which retains (or loses) activity after heating at 100 deg. C for up to 10 minutes, after reduction, and after treatment with 6 M urea;

(3) a **GDF** inhibitor identified by the methods of the invention;

(4) a **GDF** protein or peptide which inhibits **GDF** activity;

(5) a **GDF** inhibitor comprising the prodomain of a **GDF** protein, which is glycosylated;

(6) a nucleic acid (NA) selected from one of four fully defined 42 base pair (bp) nucleotide sequences (given in the specification) and which inhibits **GDF** expression when transfected in a cell;

(7) a NA selected from one of 19 fully defined 19 - 21 bp sequences (given in the specification) and which inhibits **GDF** expression when transfected in a cell;

(8) a **GDF** inhibitor comprising a variant of a **GDF** protein, which is preferably a cysteine variant, a prodomain variant, or a post-translational modification variant;

(9) a polypeptide (II) which inhibits **GDF** activity in a

cell; and
(10) a non-human animal which expresses (I).
USE - The methods are used to identify inhibitors of **growth differentiation factor** (**GDF**) proteins, especially **GDF- 8** and **GDF**-11. The inhibitors can be used to modulate **GDF-8** or **GDF**-11 activity or expression. They can be used to treat diseases or disorders characterized by aberrant expression of **GDF-8** or **GDF**-11, such as muscle-associated disorders such as cancer, muscular dystrophy, spinal cord injury, traumatic injury, congestive obstructive pulmonary disease, AIDS or cachexia, as well obesity and related disorders, disorders related to abnormal proliferation of adipocytes. They may also be used to modulate glucose transport.
ADVANTAGE - None given.
DESCRIPTION OF DRAWING(S) - The figure is a schematic representation of various **growth differentiation factor-8** (**GDF-8**) constructs. Figure 12A represents the wild type protein, figure 12B shows an uncleavable mutant with the replaced cleavage site, and figure 12C shows the pro-domain of **GDF-8**.
Dwg.12/35

FS CPI EPI GMPI
FA AB; GI; DCN
MC CPI: B04-C01C; B04-C01E; B04-E03F; B04-E08; B04-F01; B04-H06; B11-C08D1; B11-C08D2; B12-K04E; C04-C01C; C04-C01E; C04-E03F; C04-E08; C04-F01; C04-H06; C11-C08D1; C11-C08D2; D05-H09; D05-H12A; D05-H14
EPI: S03-E14H
TECH UPTX: 20000918
TECHNOLOGY FOCUS - BIOLOGY - Preferred Cells: The **GDF** inhibitor is preferably derived from medium in which CHO cells have been cultured.
Preferred Polypeptides: (II) are especially ANYCSGECEFVFLQKYPHTHLVH, KIPAMVVDRCGCS, or LSKLRLETAPNISKDVIRQLLP.
Preferred Method: The method further comprises performing electrophoresis on fractions obtained from the ion exchange and reverse phase chromatography, especially preparative non-reducing or reducing SDS-PAGE. The cells are transfected with a plasmid containing an insert encoding **GDF**, or may produce **GDF** endogenously. The testing detects the activity of a muscle-specific enzyme, especially creatine kinase. Alternatively, the testing detects adipocyte differentiation, especially of 3T3- L1 pre-adipocytes. Alternatively, the testing is performed using a transcription-based assay.
Preferred Protein: The **GDF** protein is human, or bovine, chicken, murine, rat, porcine, ovine, turkey, and baboon **GDF- 8** or **GDF**-11.
Preferred Inhibitor: (I) is a **GDF** polypeptide, especially comprising the prodomain of **GDF**. The inhibitor of (2) has a molecular weight of less than 70 kDa, and preferably does not possess **GDF-8** or **GDF**-11 activity. Preferred Method: In the method of (1), the **GDF** fragments are prepared by digesting a **GDF** protein, or synthetically prepared. The method further comprises selecting fragments which do not induce a T cell mediated response or an immune response. The **GDF** protein is digested by the use of a protease, such as trypsin, thermolysin, chymotrypsin, and pepsin. The fragments are 25 - 40 (especially 10 - 25) amino acids long.
Preferred Animal: The non-human animal of (10) is preferably a chicken, and (I) comprises the prodomain of **GDF-8** or **GDF**-11.

L132 ANSWER 3 OF 4 WPIX (C) 2002 THOMSON DERWENT
AN 2000-293165 [25] WPIX
DNC **C2000-088688**
TI Isolated nucleic acid molecule for treating cytokine-related diseases or

disorders encodes a fusion polypeptide capable of binding a cytokine to form a nonfunctional complex.

DC B04 D16
IN STAHL, N; YANCOPOULOS, G D
PA (REGE-N) REGENERON PHARM INC; (STAH-I) STAHL N; (YANC-I) YANCOPOULOS G D
CYC 88
PI WO 2000018932 A2 20000406 (200025)* EN 152p C12N015-62
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9964994 A 20000417 (200035) C12N015-62
NO 2001001513 A 20010525 (200137) C12N000-00
EP 1115876 A2 20010718 (200142) EN C12N015-62
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 2002012962 A1 20020131 (200210) C07H021-04
ADT WO 2000018932 A2 WO 1999-US22045 19990922; AU 9964994 A AU 1999-64994 19990922; NO 2001001513 A WO 1999-US22045 19990922, NO 2001-1513 20010323; EP 1115876 A2 EP 1999-952942 19990922, WO 1999-US22045 19990922; US 2002012962 A1 Provisional US 1998-101858P 19980925, US 1999-313942 19990519
FDT AU 9964994 A Based on WO 200018932; EP 1115876 A2 Based on WO 200018932
PRAI US 1999-313942 19990519; US 1998-101858P 19980925
IC ICM C07H021-04; C12N000-00; C12N015-62
ICS **C07K014-715**; C12N005-00; C12N005-02; C12N015-00; C12N015-09; C12N015-12; C12N015-63; C12N015-70; C12N015-74; C12P021-06

AB WO 200018932 A UPAB: 20000524
NOVELTY - An isolated nucleic acid molecule (I) encoding a fusion polypeptide capable of binding a cytokine to form a nonfunctional complex is new.

DETAILED DESCRIPTION - An isolated nucleic acid molecule (I) encoding a fusion polypeptide capable of binding a cytokine to form a nonfunctional complex comprises:

(a) a nucleotide sequence encoding a first fusion polypeptide component comprising the amino acid sequence of the cytokine binding portion of the extracellular domain of the specificity determining component of the cytokine's receptor;

(b) a nucleotide sequence encoding a second fusion polypeptide component comprising the amino acid sequence of the cytokine binding portion of the extracellular domain of the signal transducing component of the cytokine's receptor; and

(c) a nucleotide sequence encoding a third fusion polypeptide component comprising the amino acid sequence of a multimerizing component.

INDEPENDENT CLAIMS are also included for the following:

(1) a fusion polypeptide encoded by (I);

(2) a composition capable of binding a cytokine to form a nonfunctional complex comprising a multimer of the fusion polypeptide of (1);

(3) a vector which comprises(I);

(4) an expression vector comprising (I) operatively linked to an expression control sequence;

(5) a host-vector system for the production of a fusion polypeptide which comprises the expression vector of (4) in a host cell; and

(6) a method of producing a fusion polypeptide which comprises growing cells of the host-vector system of (5) and recovering the fusion polypeptide produced.

ACTIVITY - Anticancer; immunomodulator; osteopathic.

Mice were given subcutaneous injections of human interleukin (IL)-1 (0.3 micro g/kg). Twenty-four hours prior to human IL-1 injection, the

animals were pretreated with either vehicle or 150-fold molar excess of human IL-1 trap (0.54 mg/kg). Two hours prior to sacrifice (26 hours), the mice were given a second injection of human IL-1 (0.3 micro g/kg). Blood samples were collected at various times and sera were assayed for IL-6 levels.

Exogenous administration of human IL-1 resulted in a dramatic induction of serum IL-6 levels. At 150-fold molar excess, the human IL-1 trap completely blocked the IL-6 increase. The effects of the human IL-1 trap persisted for at least another twenty-four hours, preventing an IL-6 increase even when IL-1 was re-administered.

MECHANISM OF ACTION - The nucleic acids encode polypeptides binding a cytokine to form a nonfunctional complex.

USE - The nucleic acid and polypeptides are useful for treating cytokine-related diseases or disorders such as osteoporosis, primary and secondary effects of cancer including multiple myeloma or cachexia.

Dwg.0/73

FS CPI

FA AB; DCN

MC CPI: B04-C01G; B04-E03F; B04-E08; B04-F02; B04-F09; B04-F10; B14-H01; B14-N01; D05-H12A; D05-H12E; D05-H14A; D05-H14B1; D05-H14B2; D05-H17C1

TECH UPTX: 20000524

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Nucleic Acid: The cytokine receptor is preferably:

(a) a member of the hematopoietin family of cytokines selected from interleukin (IL)-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-9, IL-11, IL-13, IL-15, granulocyte macrophage colony stimulating **factor** (GM-CSF), oncostatin M, leukemia inhibitory **factor** and cardiotrophin-1;

(b) a member of the interferon (IFN) family of cytokines selected from IFN-gamma, IFN-alpha and IFN-beta;

(c) a member of the immunoglobulin superfamily of cytokines selected from B7.1 (CD80) and B7.2 (B70);

(d) a member of the tumor necrosis **factor** (TNF) family of cytokines selected from TNF-alpha, TNF-beta, leukotriene (LT)-beta, CD40 ligand, Fas ligand, CD27 ligand, CD30 ligand, and 4-1BBL;

(e) a member of the transforming **growth factor** (TGF)-beta/bone morphogenic protein (BMP) family selected from TGF-beta1, TGF-beta2, TGF-beta3, BMP-2, BMP-3a, BMP-3b, BMP-4, BMP-5, BMP-6, BMP-7, BMP-8a, BMP-8b, BMP-9, BMP-10, BMP-11, BMP-15, BMP-16, endometrial bleeding associated **factor** (EBAF), **growth differentiation factor** (**GDF**)-1, **GDF**-2, **GDF**-3, **GDF**-5, **GDF**-6, **GDF**-7, **GDF**-8, **GDF**-9, **GDF**-12, **GDF**-14, mullerian inhibiting substance (MIS), activin-1, activin-2, activin-3, activin-4 and activin-5; and

(f) IL-1, IL-10, IL-12, IL-14, IL-18 and MIF (macrophage inhibition **factor**).

The multimerizing component comprises an immunoglobulin derived domain selected from the Fc domain of immunoglobulin (Ig)G, the heavy chain of IgG and the light chain of IgG.

Preferred Composition: The multimer is preferably a dimer.

Preferred Host-Vector System: The host cell is preferably bacterial, yeast, insect or a mammalian cell, especially Escherichia coli, a COS cell, a Chinese hamster ovary (CHO) cell, a 293 cell, a BHK cell or an NS0 cell.

Preparation: The nucleotide sequences encoding the cytokine traps were constructed from the individual cloned DNAs by standard cloning and polymerase chain reaction techniques.

L132 ANSWER 4 OF 4 WPIX (C) 2002 THOMSON DERWENT

AN 2000-052907 [04] WPIX

DNC **C2000-013640**

TI Novel method for treating diabetes by inhibiting **GDF-8**
.

DC B04 D16
IN LIANG, L; STRASSMANN, G; TOPOUZIS, S
PA (META-N) METAMORPHIX INC; (CORR-N) CORRESTORE INC; (LIAN-I) LIANG L; (STRA-I) STRASSMANN G; (TOPO-I) TOPOUZIS S
CYC 87
PI WO 9956768 A1 19991111 (200004)* EN 49p A61K038-18
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9941832 A 19991123 (200016)
EP 1075272 A1 20010214 (200111) EN A61K038-18
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 2002031517 A1 20020314 (200222) C07H021-04
US 6368597 B1 20020409 (200227) A61K039-395
ADT WO 9956768 A1 WO 1999-US10089 19990506; AU 9941832 A AU 1999-41832 19990506; EP 1075272 A1 EP 1999-925578 19990506, WO 1999-US10089 19990506; US 2002031517 A1 Provisional US 1998-84490P 19980506, Cont of US 1999-305989 19990506, US 2001-988835 20011119; US 6368597 B1 Provisional US 1998-84490P 19980506, US 1999-305989 19990506
FDT AU 9941832 A Based on WO 9956768; EP 1075272 A1 Based on WO 9956768
PRAI US 1998-84490P 19980506; US 1999-305989 19990506; US 2001-988835 20011119
IC ICM A61K038-18; A61K039-395; C07H021-04
ICS A61K039-40; A61K039-42; **C07K016-00**; C12P021-08
AB WO 9956768 A UPAB: 20000124
NOVELTY - A method of increasing expression of GLUT4 in a subject comprising administering to the subject a **GDF-8** inhibitor.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method of increasing insulin activity and glucose uptake by cells in a subject comprising administering to the subject a **GDF-8** inhibitor; and

(2) a method of treating diabetes comprising administering to the subject a **GDF-8** inhibitor.

USE - The method can be used to downregulate GLUT4 with **GDF-8**, and to upregulate expression of GLUT4 by inhibiting **GDF-8**. This can be used to treat a variety of metabolic diseases resulting from dysfunctional glucose metabolism (e.g. hyperglycemia) and/or insulin resistance, and diabetes mellitus and related disorders such as obesity.

ADVANTAGE - Diabetes mellitus is the most common metabolic disease worldwide, and new and innovative treatment for this disease are a priority. The present invention provides such treatment.

Dwg.0/9
FS CPI
FA AB; DCN
MC CPI: B04-E06; B04-G01; B14-E02; B14-F09; B14-L06; B14-S04; D05-H11; D05-H12D2; D05-H12D4
TECH UPTX: 20000124
TECHNOLOGY FOCUS - BIOLOGY - Preferred Inhibitor: The **GDF-8** inhibitor is an antibody or antibody fragment, or is selected from a **GDF- 8** peptide fragment (derived from mature **GDF-8** protein or form the Pro domain of **GDF-8**), a dominant-negative mutant of **GDF-8**, a **GDF-8** receptor antagonist, a non-**GDF-8** peptide, an antisense nucleic acid or a ribozyme.

Preferred Method: Insulin sensitivity and glucose uptake is increased by modulating the expression of a hexose transporter selected from GLUT4 and GLUT1, and the cell is a muscle cell or adipocyte, or precursor thereof.

=> d his

(FILE 'HOME' ENTERED AT 13:28:25 ON 03 JUN 2002)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 13:28:47 ON 03 JUN 2002
L1 72 S GDF8 OR (GDF OR GROWTH DIFFERENTIAT? FACTOR)()8

FILE 'REGISTRY' ENTERED AT 13:29:14 ON 03 JUN 2002
L2 1 S 271597-12-7

FILE 'HCAPLUS' ENTERED AT 13:29:26 ON 03 JUN 2002
L3 24 S L2
L4 72 S L1,L3
E KLYSNER S/AU
L5 8 S E3,E4
E MOURITSEN S/AU
L6 44 S E3-E5
E HALKIER T/AU
L7 69 S E3,E4
E PHARMEXA/PA,CS
L8 4 S E3-E8
E "M AND B"/PA,CS
E "M AND E"/PA,CS
L9 5 S E5-E9
L10 26 S (M(L)"E"(L)BIOTECH?)/PA,CS
L11 14 S (M(1W)"E"(L)BIOTECH?)/PA,CS
L12 14 S L9,L10 AND L11
L13 15 S L9,L11,L12
L14 12 S L10 NOT L13
L15 2 S L4 AND L5-L7
L16 0 S L4 AND L8
L17 1 S L4 AND L13
L18 2 S L15,L17
E DK99-1014/AP,PRN
L19 1 S E4
E US99-145275/AP,PRN
L20 1 S E5
L21 2 S L18-L20

FILE 'REGISTRY' ENTERED AT 13:37:37 ON 03 JUN 2002
E GROWTH/DIFFERENTIATION FACTOR/CN
L22 50 S E55-E104
L23 132 S GROWTH DIFFERENTIATION FACTOR 8
L24 82 S L23 NOT L2,L22
L25 27 S L24 AND PROTEIN/FS
L26 76 S L22,L23 AND PROTEIN/FS
L27 55 S L22-L25 NOT L2,L26

FILE 'HCAPLUS' ENTERED AT 13:40:18 ON 03 JUN 2002
L28 21 S L26
L29 15 S L27
L30 1 S L28,L29 AND L5-L7,L13
L31 2 S L21,L30
L32 76 S L4,L28,L29
L33 46 S L32 AND (PD<=19990726 OR PRD<=19990726 OR AD<=19990726)
L34 4 S L33 AND CARRIER
E DRUG DELIVERY/CT

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                E E5+ALL
L35           8 S E3,E2+NT AND L33
L36           0 S E342+NT AND L33
L37           1 S E340+NT AND L33
                E E340+ALL
                E E12+ALL
L38           0 S E8+NT AND L33
L39           1 S L33 AND DOWN(L)REGULAT?
                E VACCINE/CT
                E E4+ALL
L40           3 S E4 AND L33
L41           5 S E8+NT AND L33
L42           0 S E10+NT AND L33
L43           0 S E11+NT AND L33
L44          13 S L31,L34,L35,L37,L39-L41
                E MUTATION/CT
                E E3+ALL
L45           8 S L33 AND E1+NT
L46          19 S L44,L45
                E TOXOID/CT
                E E4+ALL
L47           1 S L33 AND E4+NT
L48           3 S L33 AND E3+NT
L49           3 S L33 AND (E8+NT OR E9+NT)
L50          19 S L46-L49
L51          10 S L50 AND GROWTH DIFFERENTIAT? FACTOR
L52          15 S L50 AND GDF?
L53          17 S L51,L52
L54           2 S L50 NOT L53
L55          44 S MYOSTATIN? AND L32
L56          20 S L55 AND L33
L57           1 S L56 AND L31
L58          43 S MYOSTATIN? AND (PD<=19990726 OR AD<=19990726 OR PRD<=19990726

     FILE 'REGISTRY' ENTERED AT 13:53:26 ON 03 JUN 2002
L59         161 S MYOSTATIN?
L60         126 S L59 NOT L2,L22-L27

     FILE 'HCAPLUS' ENTERED AT 13:53:53 ON 03 JUN 2002
L61          14 S L60
L62          27 S L59
L63          27 S L61,L62
L64          18 S L63 AND (PD<=19990726 OR AD<=19990726 OR PRD<=19990726)
L65           5 S L64 AND L50
L66          32 S L50-L54,L56,L57,L65
L67          38 S L33,L58,L64 NOT L66
L68           8 S (L2 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27  OR L59)(L)THU/
L69           7 S L68 AND L66
L70           1 S L68 AND L67
L71           9 S 15/SC,SX AND L33,L58,L64
L72          34 S L69,L71,L66
L73          36 S L67 NOT L72
L74         116 S GROWTH(S)DIFFERENTIATION(S)FACTOR(S)8
L75          76 S L74 AND (PD<=19990726 OR PRD<=19990726 OR AD<=19990726)
L76          47 S L75 NOT L33,L58,L64
L77          19 S L74 AND L72
L78          34 S L72,L77
L79          21 S L78 AND GROWTH(L)DIFFERENTIATION(L)FACTOR
L80          13 S L78 NOT L79
                SEL DN 4 7 9
L81           3 S E1-E3 AND L80
                SEL DN 1 7 9 11 15 16 21 L79
L82          14 S L79 NOT E4-E10
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L83          16 S L81,L82 AND GROWTH(L)DIFFERENT?(L)FACTOR
L84          17 S L81,L82 AND L1,L2-L21,L28-L58,L61-L83
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 15:00:02 ON 03 JUN 2002
L85         145 S E11-E155
L86           1 S L85 AND L2
L87          42 S L85 AND L22-L27
L88         109 S L85 AND L59,L60
L89         113 S L87,L88 AND PROTEIN/FS
L90          21 S L89 AND GROWTH(L)DIFFERENTIATION(L)FACTOR(L)8/CNS
L91          92 S L89 NOT L90
L92          31 S L85 NOT L86,L89-L91
L93          20 S L92 AND GROWTH(L)DIFFERENTIATION(L)FACTOR(L)8/CNS
L94          11 S L92 NOT L93
L95          18 S L93 NOT MYOSTATIN/INS.HP
L96          40 S L90,L95,L86
L97          38 S L96 NOT MYOSTATIN/INS.HP
L98          37 S L97 NOT L86

     FILE 'REGISTRY' ENTERED AT 15:06:26 ON 03 JUN 2002

     FILE 'HCAPLUS' ENTERED AT 15:06:38 ON 03 JUN 2002

     FILE 'BIOSIS' ENTERED AT 15:07:10 ON 03 JUN 2002
L99          38 S L1 OR L2 OR L22-L27 OR L60
L100       1464 S L74
L101       1847 S GROWTH(S)DIFFERENTIAT?(S)FACTOR(S)8
L102       1863 S L99-L101
L103       1465 S L102 AND PY<=1999
                E KLYSNER S/AU
L104          0 S E3,E4 AND L103
                E MOURITSEN S/AU
L105          0 S E3,E4 AND L103
                E HALKIER T/AU
L106          0 S E3,E4 AND L103
L107          0 S L102 AND (KLYSNER S? OR MOURITSEN S? OR HALKIER T?)/AU

     FILE 'MEDLINE' ENTERED AT 15:10:18 ON 03 JUN 2002
L108       1468 S L103
                E GROWTH DIFFERENTIATION FACTOR/CT
                E GROWTH SUBSTANCES/CT
                E E3+ALL
L109      18832 S E24
L110         75 S L109/MAJ AND L108
L111          0 S L110 AND GDF8
L112          0 S L110 AND GDF 8
L113          0 S L110 AND GROWTH DIFFERENTIAT? FACTOR 8
L114          0 S L110 AND GROWTH(1W) DIFFERENTIAT? FACTOR 8
L115          0 S L110 AND FACTOR 8
L116         11 S L108 AND (GDF8 OR GDF 8)
L117          4 S L108 AND GROWTH DIFFERENTIAT? FACTOR 8
L118          5 S L108 AND GROWTH(5W)DIFFERENTIAT? FACTOR 8
L119          5 S L108 AND GROWTH(5W)DIFFERENTIAT?(5W)FACTOR 8
L120         13 S L116-L119
                SEL DN 2
L121          1 S L120 AND E1-E2

     FILE 'MEDLINE' ENTERED AT 15:17:05 ON 03 JUN 2002

     FILE 'WPIX' ENTERED AT 15:17:13 ON 03 JUN 2002
L122         19 S L1
L123         65 S GROWTH(S)DIFFERENTIAT?(S)FACTOR(S)8
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L124          12 S L122 AND L123
L125          19 S L122,L124
L126          12 S L125 AND C07K/IC,ICM,ICS
L127           7 S L125 NOT L126
                 SEL DN 5 7 8 10 L126
L128           4 S L126 AND E3-E7
L129           4 S L122-L127 AND L128
L130           3 S L129 AND GROWTH(L)DIFFERENTIAT?(L)FACTOR
L131           4 S L129 AND GDF?
L132           4 S L130,L131

     FILE 'WPIX' ENTERED AT 15:26:18 ON 03 JUN 2002
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No.	Doccode	Number of pages
1	A...	3
2	CLM	1
3	REM	4
4	SEQLIST	30

Total number of pages: 38

Remarks:

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